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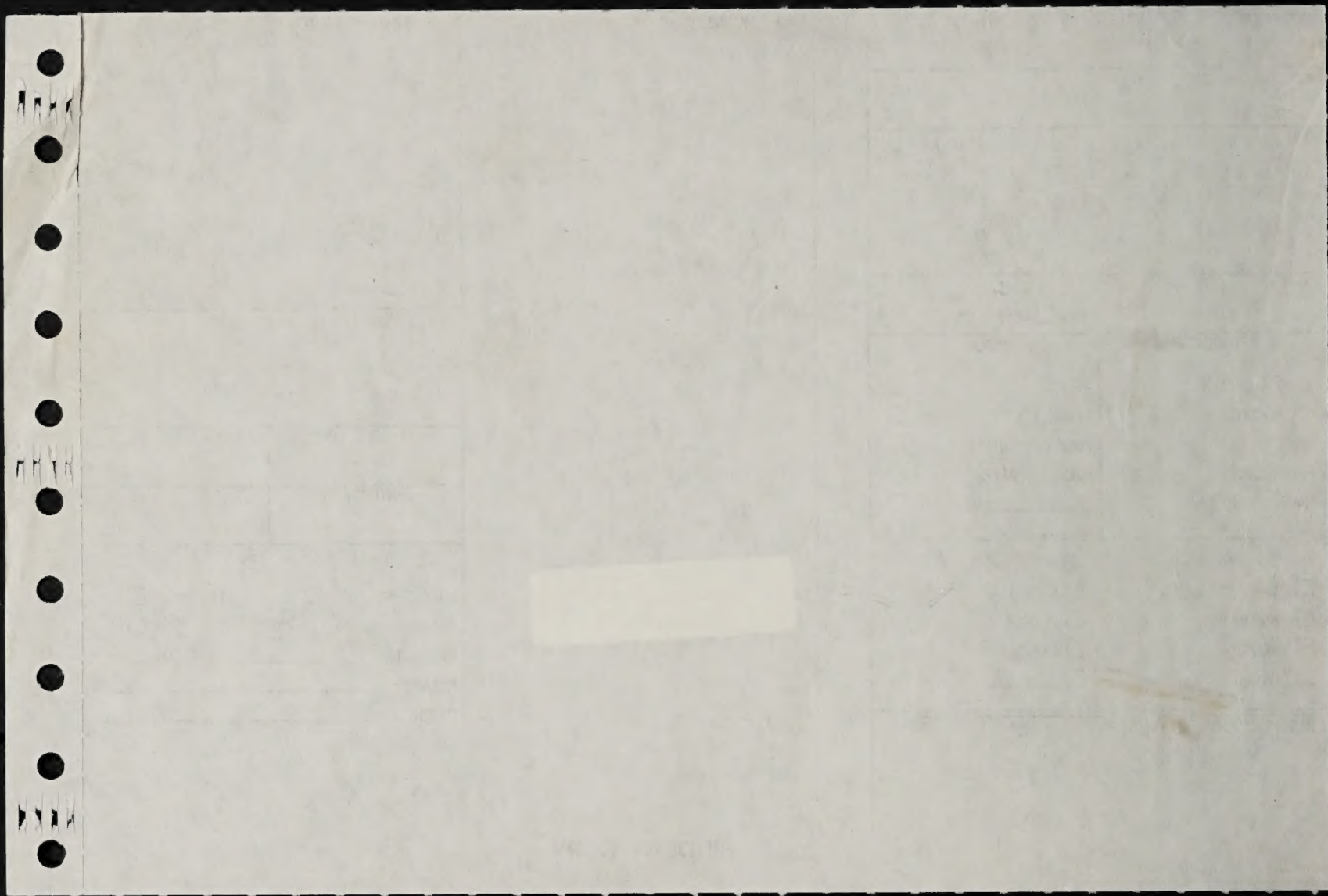
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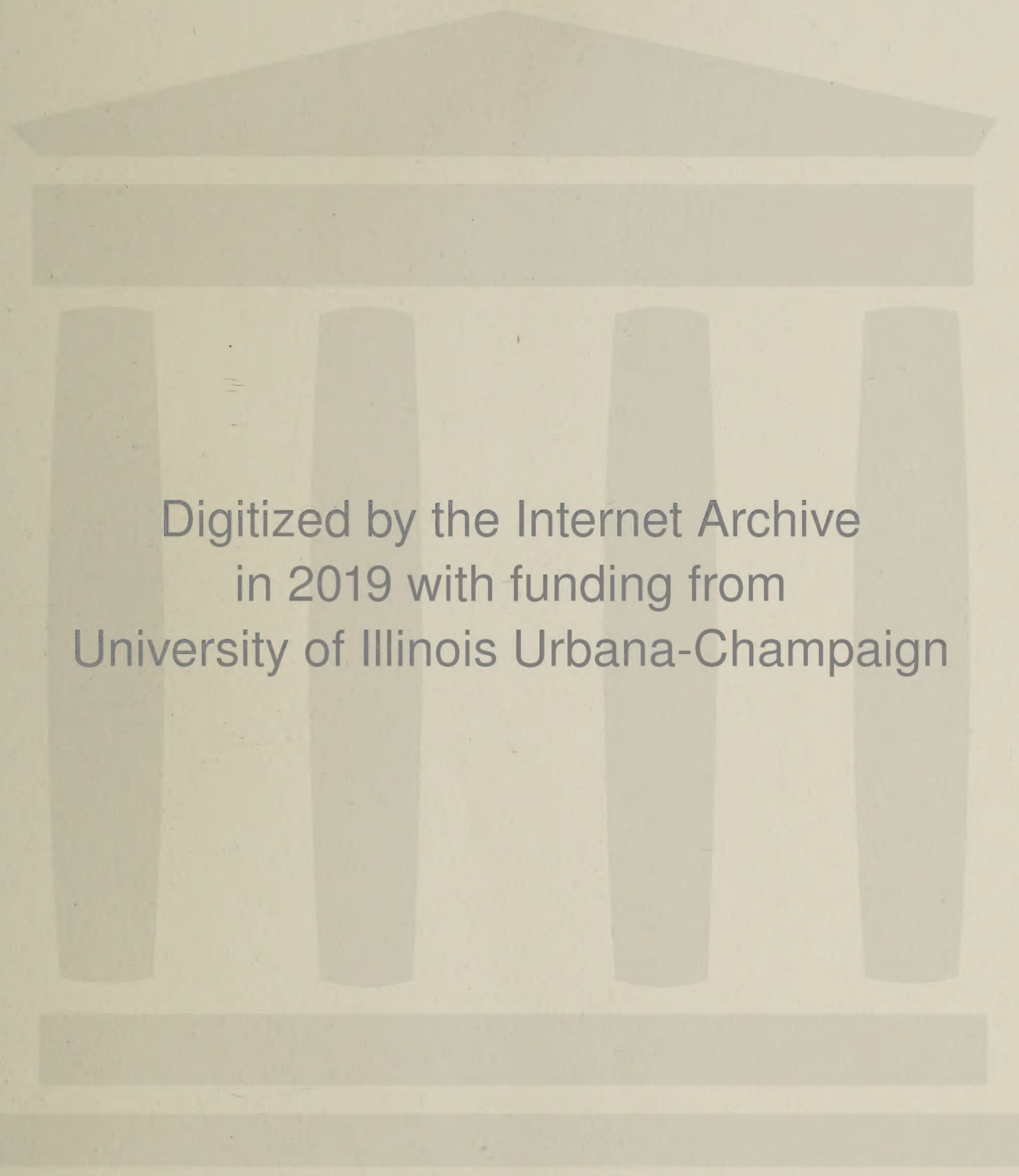
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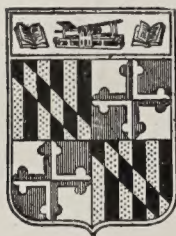
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VOLUME XXVIII

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RELATION OF TONSILLAR AND NASOPHARYNGEAL INFECTIONS TO GENERAL SYSTEMIC DISORDERS.¹

By S. J. CROWE, S. SHELTON WATKINS and ALMA S. ROTHHOLZ.

(From the Department of Laryngology, Rhinology and Otology of The Johns Hopkins University and Hospital.)

In order to determine the relation of tonsillar and nasopharyngeal infections to various general disorders, we have followed up and examined, subsequent to their discharge from the hospital, as many as possible of the patients from each of the following groups:

I. Arthritic group:

1. Removal of tonsils as a therapeutic measure for infectious arthritis.
2. Removal of tonsils as a therapeutic measure for rheumatoid arthritis.
3. Removal of tonsils as a therapeutic measure for myalgia or myositis.
4. Removal of tonsils as a therapeutic measure for acute rheumatic fever.

II. Removal of tonsils as a therapeutic measure for chorea.

III. Removal of tonsils as a therapeutic measure for neuritis.

IV. Removal of tonsils as a therapeutic measure for hyperplasia of the cervical glands.

In addition to the tabulation and discussion of the material of these seven groups, we also include a general discussion of each of the following subjects:

- A. The clinical anatomy of the nose, throat and lymphatic system in the neck.
- B. Focal infection with reference particularly to the tonsils and nasopharynx.
- C. The portals of entry of tubercle bacilli, and a report on city-six cases of an "apparently primary" tuberculosis of the tonsils or adenoids found in our series.
- D. The indications and contra-indications for tonsillectomy.

E. The operation and the post-operative complications of tonsillectomy.

These discussions are included particularly for the benefit of the students in the third and fourth years of the medical school.

Introduction.—The reorganization of the Nose, Throat and Ear Department of The Johns Hopkins Hospital in 1911, on what was practically a full-time basis, rendered it possible to make more careful general physical examinations of the patients in this department before operation; to carry out the operative procedures under the best conditions for both the patient and the operator; to make routine histological examinations of the tissues removed at operation; and to establish a system for following up the more interesting cases after their discharge from the hospital.

Every operative case, with the exception of the simple adenoidectomies, is admitted to the surgical wards of the hospital. A routine physical examination is made before the operation, and the patients are not discharged until all danger of post-operative complications is past.

The greatest benefit derived from this arrangement, however, is the spirit of co-operation between the laryngological and other departments. Previous to 1911, practically all operations on tonsils, sinuses, and even mastoids were done in the out-patient department, with the aid of inexperienced anaesthetists and assistants; and, as a rule, the patients were sent to their homes a few hours later. Under these conditions, but few of the interesting cases with cardiac, renal or arthritic symptoms secondary to a focal infection in the tonsils or sinuses were referred by the other departments. Since 1911, however, we have had an opportunity to operate on and subsequently follow up a large number of cases with some general systemic disorder, supposed to be secondary to a chronic focus of infection in the upper air passages.

¹Based on the study of 1000 cases operated on at The Johns Hopkins Hospital during the past five years.

This report is based on the study of 1000 tonsillectomies. A histological examination of the tonsils and adenoids removed at operation was made in every case. *We include in the tables and in the text, only those patients concerning whom we have some definite information as to what benefit, if any, resulted from the removal of their tonsils.* The post-operative data were obtained partly through the courtesy of the family physician; partly by letters from the patients themselves; but chiefly by personal examinations of the patients brought back by a special social service nurse² from one to four years after their discharge from the hospital. It is our intention to re-examine each year the patients included in the following tables, and to report again on their condition after five years. It will be particularly interesting to see how often there is a recurrence of chorea, rheumatic fever, arthritis, and renal symptoms in these patients who now have their upper air-passages in good condition. It will also be of interest to determine the ultimate result in the forty-six patients who had an "apparently primary" tuberculous lesion in either the tonsils or adenoids.

On account of the large number of nose, throat and ear cases treated in the out-patient department and in the hospital, and our small staff of assistants, the records in many instances are not so complete as we would wish. This is particularly true of the group of tuberculous tonsils or adenoids. In the great majority of cases in this group, a tuberculous lesion was not suspected at the time of the operation, but was only discovered by the routine histological examination of the tissue removed at operation.

It is a difficult matter to obtain post-operative notes and examinations on these patients. Many of the patients admitted from the out-patient department deliberately give false addresses, and many others are foreigners or negroes who frequently change their place of residence.

Although the records are incomplete in some essential details, we believe they are interesting enough to publish in full, since they tend to support the evidence of Billings and others in regard to the importance of focal infections in many of the general disorders seen by the internist, the pediatrician and the general surgeon.

A. CLINICAL ANATOMY OF THE NOSE, THROAT AND THE LYMPHATIC SYSTEM IN THE NECK.

For purposes of description, the pharynx is divided into three portions: The nasopharynx, the oropharynx and the laryngopharynx.

The Nasopharynx.—The nasopharynx with its local collection of lymphoid tissue, variously spoken of as the pharyngeal tonsil, third tonsil, Luschka's tonsil, adenoids, post-nasal growths, etc., is of importance from many points of view. Not infrequently maladies of children are referable either directly

or indirectly to the abnormalities or infections of the nasopharynx.

Obstruction in this locality results in mouth-breathing with its familiar indirect effects. The most common results are stasis of nasal secretions with excoriation of the skin around the external nares; frequently an accessory nasal sinus infection; changes in the facial expression: retardation of mental and physical development; defective speech; affections of the ear, both suppurative and catarrhal;³ also numerous symptoms, usually described as "reflex neuroses." Among these, night terrors, asthma, petit-mal-like attacks, paroxysmal nocturnal attacks of coughing, and enuresis nocturna are the most common. A further possible result of enlarged adenoids is an interference with the development of the superior maxillary bones which results in a high, narrow V-shaped deformity of the hard palate.

The anatomical landmarks of the nasopharynx as seen in the post-nasal mirror are: (1) the orifices of the nasal passages in which can be seen the posterior ends of the turbinates or conchæ; (2) the pharyngeal orifices of the Eustachian tubes; (3) the fossa of Rosenmueller just behind the Eustachian orifice on each side; (4) the mound of lymphoid tissue (adenoids) on the vault, most prominent in the median line, but often extending laterally or hanging down sufficiently to obstruct the posterior nasal orifices and the openings of the Eustachian tubes.

The anterior lobe of the hypophysis cerebri is developed from an infolding of the mucous membrane of the vault of the nasopharynx, known as the pouch of Rathke. In young animals and children, "rests" of anterior lobe cells may be found along the embryological pathway from the nasopharynx to the sella turcica.⁴ In some respects, this pathway in adult life is similar to the thyro-glossal duct.

The nasopharynx has a rich blood supply. The pharyngeal branches of the vidian and pterygo-palatine arteries anastomose with the ascending pharyngeal. The veins empty into the pterygoid plexus.

Spontaneous bleeding from the nasopharynx in children is not an infrequent symptom of enlarged adenoids. The blood may come from one or both nostrils, from the mouth, or may be swallowed. When it is reported that blood is found on a child's pillow, it is probably a symptom of adenoids.

Other common sources of bleeding in the nose and throat are:

1. Superficial, non-specific ulceration on the anterior third of the septum, perhaps the most common.
2. Ulceration in the posterior nares or nasopharynx, secondary to a coryza or nasopharyngitis. Bleeding from this source may become quite serious in adults unless properly treated.⁵

³ It has been estimated that eighty per cent of the deaf adults in the United States owe the origin of their trouble to neglected nasopharyngeal disorders in childhood.

⁴ Haberfeld: Die Rachendachhypophyse, etc., Beitr. z. path. Anat. u. z. allg. Path., 1910, XLVI, 133-232.

⁵ Spontaneous bleeding from the posterior nares or nasopharynx, aside from a new growth or leukæmia, is usually the result of an infection. In treating patients with a severe bleeding from this locality, it is of the greatest importance to bear in mind the local conditions that cause the hemorrhage. The mucous membrane

² In justice to the regular Social Service Department of the hospital, it should be mentioned that they do not spend their time in looking up or bringing back for examination tonsils cases that have been operated on several years previously. This work is done by a nurse employed by us for this particular purpose.

3. Spongy gums associated with pyorrhea alveolaris in adults, and the granulations in carious molar teeth in children.

4. Enlarged veins around the base of the tongue, said to be a particularly common source of bleeding in gouty persons.

5. Nasal diphtheria; various blood diseases; vicarious menstruation; new growths and œsophageal varices.

6. Foreign bodies should always be suspected when there is a long continued oozing of blood from the nose or throat in young children. Within the past year, an infant seven months of age, was admitted to the Pediatric clinic of The Johns Hopkins Hospital with a history of frequent vomiting of bright red blood, and tarry stools for two weeks. Hemoglobin was 45 per cent, but, otherwise, the child was in excellent condition. Although the parents very much resented the suggestion that the child might have swallowed a foreign body, an X-ray plate was made and an open safety-pin, point up, was found in the upper third of the œsophagus. After removal, all bleeding ceased and the child made an uninterrupted recovery.

7. When there is blood-tinged expectoration in adults and children over twelve years of age, pulmonary tuberculosis should be suspected, and a thorough examination of the lungs and sputum should be made.

There is a close mesh of lymph vessels in the vault of the nasopharynx. They drain either into the the retropharyngeal glands or into the posterior or external group of the deep lateral chains in the neck.

Retropharyngeal abscesses, so common in young children, are probably due to a suppurative adenitis secondary to nasopharyngeal infection. The retropharyngeal glands of Henle are situated on each side of the median line between the mucous membrane of the pharynx and the aponeurosis over the bodies of the second and third cervical vertebræ. These glands receive the lymphatics of the pharynx, nasopharynx, nose, Eustachian tubes and middle ear. They undergo atrophic changes between the third and fifth years.

Primary tuberculosis of the adenoids is not infrequent. Routine histological examination of the tonsils and adenoids from 1000 cases operated on at The Johns Hopkins Hospital revealed 14 cases with an "apparently primary" tuberculosis of the adenoids. These cases are given in detail in the table of tuberculous tonsils and adenoids. We have repeatedly noted

and surrounding lymphoid tissue are infected, and, as a rule, there is a long-standing infection of one of the accessory nasal sinuses. It is against all the principles of surgery to pack this infected area and to leave the packs in place for a week or longer, as is usually recommended in text-books.

The bleeding begins as a result of an ulceration of the mucous membrane and the erosion of an artery or vein. Packing such an infected area without frequent removal and cleansing, only encourages an extension of the ulceration, and makes it more difficult to control the bleeding. The packing employed should be of sterile gauze and as small and compact as possible. If the nasopharynx is packed, the packing should be removed at least once every forty-eight hours, and the nose and mouth thoroughly washed with a sterile salt or alkaline solution. This should be done even though the bleeding starts again when the packs are removed. The pressure alone of a nasopharyngeal pack, held in place by tape coming through the anterior nares, will cause ulceration. The mouth and anterior nares must be kept as clean as possible by washes and irrigation with some sterile, non-irritating fluid.

that *bilateral* tuberculous cervical adenitis is associated with a tuberculous lesion in the adenoids alone. On the other hand, *unilateral* tuberculous involvement of the cervical glands is frequently associated with a tuberculous process in the tonsil on the affected side, the other tonsil and the adenoids being free from any microscopical tuberculous lesion.

It is difficult to determine at what stage an amount of adenoid tissue ceases to be physiological. We do not advise the removal of adenoids or tonsils in all children, solely because of their size. In this clinic, the practice is to regard the tonsils and adenoids as physiologically important parts of the mechanism that protects the lower air passages from dust and organisms. This will be more fully discussed in connection with the indications for tonsillectomy. If there is no mouth-breathing; no evidence of damage to the ears; no chronic enlargement of the glands of the neck; no cystic condition of the adenoids known as Thornwaldt's disease; and none of the so-called "reflex neuroses," we do not recommend the removal of adenoids regardless of their size or appearance.

There is normally a hyperplasia of the tonsils and adenoids between the ages of three and twelve years. The Hebrew race is especially predisposed to this hyperplasia. Climate is also a predisposing factor. Osler is of the opinion that there are more mouth-breathers to the acre in England than in any other country, while Massei in Naples reports that he has seen only five cases during the past fifteen years in which an adenoidectomy was indicated. In Baltimore, about 25 per cent of the children visiting the various out-patient departments have some definite indication for removal of their adenoids, the most common being frequent attacks of otitis media.

The Oropharynx.—The oropharynx is that portion of the pharynx lying between the free edge of the soft palate and the upper border of the epiglottis. It contains the tonsils and a variable amount of lymphatic tissue in the mucous membrane of the lateral and posterior walls.

As to the function of the tonsils, adenoids and other lymphatic tissue in the throat, we assume that it is a part of the mechanism for the protection of the lower air passages against infection.

There are three protective agencies in the upper air passages:

1. The mucus secreted by the mucous membrane of the nose, pharynx and trachea.
2. The ciliated epithelium of the nasal and tracheal mucous membrane.
3. Waldeyer's ring of lymphoid tissue in the throat, together with the lymphatic glands of the neck.

The mucus is an important factor in protecting the lower air passages from bacteria and dust. Under normal conditions of life in large cities, from 15,000 to 20,000 bacteria enter the nose during an hour's quiet respiration. With normal anatomical and physiological nasal conditions, but few of these organisms ever reach the nasopharynx in a viable condition. This is due partly to the relatively large amount of mucus secreted by the nasal mucous membrane—over a liter in

24 hours⁶—and partly to the fact that this mucus is inhibitory if not actually bactericidal.⁷

Interference with the function of the ciliated epithelium of the trachea is well illustrated by the distress in whooping cough.⁸ Highly specialized epithelium is equally important in the nose. When destroyed by caustics, operative procedures or disease, the ciliated cells are replaced by squamous cells, and the efficiency of the nose as a protective organ is impaired.

The tonsil is probably the principal portal of entry for the infections following contamination of the mouth with soiled hands or toys, infected food, milk or water. Wood⁹ has found that the tonsils in the hog are more readily infected by the anthrax bacillus than is any other portion of the buccal or pharyngeal mucous membrane. From his experiments he concludes that the anthrax bacillus passes through the epithelium lining the crypts and not the surface mucosa; and that the organisms gain entrance to the parenchyma of the tonsil by passing through living, unaltered epithelium.

There is both experimental and clinical evidence, however, that organisms can pass through the intact mucous membrane¹⁰ and lymphoid tissue of the pharynx. Clinically, we have frequently seen arthritic symptoms reappear and the cervical glands become enlarged and tender as the result of a simple pharyngitis in patients whose tonsils and adenoids had been thoroughly removed.

That organisms may pass through intact mucous membrane and leave no evidence of local injury, has been best worked out for the tubercle bacillus.¹¹ Living bacilli may be recovered from the lymph stream within a few minutes after the introduction of a suspension of tubercle bacilli into the gastrointestinal tract of a normal animal, either by stomach-tube or by rectal injection.

Harbitz,¹² in 1905, made a careful study of the glandular system in a large number of clinically tuberculous and non-tuberculous persons coming to autopsy. His object was to determine as far as possible the primary portal of entry in those with tuberculous lesions of the lungs, glands, bones and meninges. In many instances, he demonstrated by animal inoculation and by cultural methods, tubercle bacilli in tonsils, ad-

enoids and cervical glands that grossly and microscopically showed no tuberculous lesion. In general, these results have been confirmed by other observers, and it is probable that tubercle bacilli may not only pass through normal mucous membrane without causing any local lesion, but may remain latent in histologically normal lymph glands for months or years.

The tonsils are composed of lymphatic cells with follicles or germinal centers as in an ordinary lymph gland. They differ from lymph glands in that they have only efferent lymph channels, and no medullary sinuses. The invaginations of the surface epithelium form deep crypts known as fossulae. These crypts are the most important anatomical characteristic of the tonsils. They develop from an ingrowth of squamous epithelium, their lumina being formed by the desquamation of a central core. The cells lining the crypts have no sub-epithelial layer of connective tissue. The crypts extend, as a rule, through the entire thickness of the tonsil and end blindly at the fibrous capsule. Under normal conditions they contain desquamated epithelial cells, lymphoid cells and particles of food. Anything that tends to obstruct the orifices of the crypts produces a stasis and an increased susceptibility of the tonsil to infection. It is probable that acute tonsillitis usually begins as one or more focal abscesses in partially obstructed crypts; certainly, it may often be aborted during the early stage by irrigation of the infected crypts with salt solution or sterile water.¹³

During the act of swallowing, saliva and food are forced into the crypts together with any organisms that may be in the mouth. This is of importance in the etiology of both acute and chronic tonsillar infections. During childhood the mouth is frequently contaminated by soiled hands, toys, impure water or food, and milk infected with pyogenic organisms or bovine tubercle bacilli. In some persons, these factors may produce an acute angina; in others, chronic inflammatory changes. Sometimes a hyperplasia of the lymphoid elements of the tonsil results, and, less frequently, a proliferation of the connective tissue. In either case, the efficiency of the tonsil as a protective organ is decreased.

It has been mentioned that with normal nasal passages but few, if any, organisms entering the nose ever reach the nasopharynx in a viable condition. If, however, there is a partial nasal obstruction with a stasis of secretions; or if infected discharges are draining into the nasal cavity from the conjunctivæ, accessory nasal sinuses or middle ear, the nasopharynx, pharynx, tonsils and larynx are constantly bathed in a discharge that is irritating and contains bacteria. In the same way the tonsil may become chronically infected, or, at least, less resistant to an acute infection, when there is a discharging alveolar abscess, an infection under a crowned tooth, carious teeth or an extensive pyorrhea.¹⁴

⁶ Bloch, E.: *Physiological Investigations of Nasal Respiration*. (Translated and abridged by S. DeJager and F. Cohn); Arch. Otol. N. Y., 1888, XVII, 279-307; 1889, XVIII, 1-24.

⁷ Thompson and Hewett: *The Fate of Micro-organisms in Inspired Air*; Lancet, Lond., 1896, I, 86.

⁸ Mallory: *Pertussis; The Histological Lesion in the Respiratory Tract*; J. Med. Research, 1912, XXVII, 115-123.

⁹ Wood, G. B.: *Tonsillar Infection*; Am. J. M. Sc., 1914, N. S. CXLVII, 380-388.

¹⁰ von Klecki, K.: Bericht über die im Institute angestellten experimentellen Untersuchungen über den Durchtritt von Bakterien durch die intakte Darmschleimhaut; Festschr. enthält. Arb. u. Tuberk., XXXVI, Internat. Tuberk.-Konf., 1907, 31-33. Also Wien. klin. Wchnschr., 1907, XX, 1107-1108.

¹¹ Wright, J.: *Some Critical and Desultory Remarks on Recent Laryngological and Rhinological Literature*; N. York M. J. (etc.), 1900, LXXI, 504-508.

¹² Harbitz, F.: *Untersuchungen über die Häufigkeit, Lokalisation und Ausbreitungswege der Tuberkulose*; Kristiania, 1905.

¹³ For irrigating the crypts, a blunt, large-bore needle bent at right angles about 1 cm. from the end is attached to an ordinary syringe.

¹⁴ Bass and Johns: *Pyorrhea Dentalis and Alveolaris*; J. Am. M. Ass., 1915, LXIV, 553-558.

Aside from the changes in the lymphoid tissue in the throat, large numbers of organisms probably get through to the cervical glands and there produce changes in the medullary sinuses that render these glands more liable to infection and less resistant, during an acute angina, to the passage of organisms to the blood stream.

It is also our impression from clinical observation that partial occlusion of the crypts resulting from an incomplete tonsillectomy renders the patient more liable to secondary cardiac, joint or renal lesions. During the past four years, we have seen eight cases with an infectious arthritis and an evening elevation of temperature of several months' duration that illustrate this point well. In every case, there was a history of frequent attacks of tonsillitis for many years preceding, but never with anything but local symptoms. With the idea of stopping these acute attacks, each of these patients had had a partial tonsillectomy. Local anæsthesia had been used in all. In some, the tonsils were removed with a guillotine; in others with an electric cautery. All went well until the next coryza, following which the joint symptoms appeared for the first time. Searching for a portal of entry, portions of the tonsils were found with crypts obscured by scar tissue. After their removal, the joint symptoms gradually disappeared and the temperature returned to normal. What we wish to emphasize is that the partial tonsillectomy, by narrowing the orifices of the crypts of the remaining portion of the tonsil, mechanically made the conditions more favorable for a general infection. Frequently the joint symptoms in such cases will not clear up after a tonsillectomy, presumably owing to the fact that the cervical glands have also become foci of infection.

The palatine tonsil is situated in a fossa between the glosso-palatine and pharyngopalatine arches. The glossopalatine arch (anterior pillar of the fauces) contains the glossopalatine muscle, and the pharyngopalatine arch (posterior pillar) contains the pharyngopalatine muscle. During deglutition, the contraction of these muscles compresses the tonsil and, under normal conditions, forces the detritus out of the crypts. When the orifices of the crypts are partially occluded, however, this pressure by the arches tends to force organisms and other foreign material into the parenchyma of the tonsil.¹⁵

A distinct fibrous capsule separates the tonsil from the surrounding structures. This capsule is a particularly important landmark. Whatever the technique employed in removing the tonsil, the two essentials are: (1) removal of the tonsil together with its entire capsule; (2) control of hemorrhage. If a portion of the capsule remains, it means an incomplete tonsillectomy, and frequently subsequent histories of patients indicate that such operations do more harm than good.

The blood supply of the tonsil is derived from the following sources:

1. The tonsillar ramus of the external maxillary artery. It is important to remember that the main trunk of the external maxillary artery, after leaving the external carotid, may take

a decided upward bend before it passes around the ramus of the jaw. The loop thus formed comes in close relation to the inferior portion of the tonsil, and in removing a tonsil, this large artery may be cut unless the field of operation is kept dry and the dissection made as close as possible to the capsule.

2. A large branch of the lingual artery enters near the inferior extremity of the tonsil behind. In order to do a complete tonsillectomy, we have found it necessary to ligate this vessel in every case, both in adults and children.

3. The upper portion of the tonsil is supplied by one of the pharyngeal rami of the ascending pharyngeal artery and by the descending palatine artery—a branch of the internal maxillary.

The nerve supply is mainly through the glosso-pharyngeal.

The lymphatic drainage of the tonsil has been worked out best by Wood.¹⁵ The *tonsil gland* is described as one of the group of deep cervical glands; it lies just beneath the anterior border of the sternomastoid muscle, where it is crossed by the posterior belly of the digastric muscle. It lies external from and slightly anterior to the internal jugular vein; is embedded in loose areolar tissue; and when enlarged, is dislocated outward and forward, presenting at the angle of the mandible.

In order to have a clear understanding of the diseases of the nasopharynx and tonsils and their complications, it is necessary briefly to review the anatomy of the various groups of lymph glands in the neck.

There are two methods by which a lymph gland may become infected. One is by a retrograde thrombosis of the efferent lymph vessels; the other and most common way is through the afferent lymph stream. Anatomically, there are but few, if any direct communications between the cervical lymphatics and the supra-clavicular, axillary, bronchial or mediastinal groups. This fact is also borne out by clinical findings, since practically all the pathological conditions of the cervical glands are secondary to some infection by, or growth in, the mouth, nose, throat or scalp.

The neck on each side is divided by the sternocleidomastoid muscle into an anterior and a posterior triangle. The anterior triangle is subdivided into the submaxillary triangle, bounded below by the digastric muscle and into the two carotid triangles; the superior (above the level of the cricoid cartilage), and the inferior, below the anterior belly of the omohyoid muscle. The posterior triangle is divided by the posterior belly of the omohyoid into the occipital and supraclavicular (or subclavian) triangles.

The arrangement of the lymphatic glands of the neck is as follows:

- I. A group of collecting nodes that forms a kind of collar about the upper portion of the neck. These consist of:

1. *Occipital glands*, which drain the adjoining portion of the hairy scalp.

2. *Mastoid or posterior auricular glands*, which drain a portion of the scalp, auricle, and a portion of the posterior wall of the external auditory canal.

¹⁵ Wood, George B.: The lymphatic Drainage of the Faucial Tonsils; Am. J. M. Sc., 1905, CXXX, 216-227.

¹⁵ Loc. cit.

3. *The parotid group* receives afferent vessels from the drum, anterior wall of the external auditory canal, cheek, temporal portion of the scalp and possibly the conjunctival sac.

4. *The submaxillary group* drains the cheek, a portion of the external nose, gums, lateral and anterior part of the tongue, and all the lower lip except its central portion.

5. *The submental glands* are situated in the triangle bounded by the anterior bellies of the two digastric muscles and the hyoid bone. The afferent vessels of this group are from the chin, middle of the lower lip, tip of the tongue and adjoining portion of gums and floor of the mouth.

6. *The retropharyngeal glands* receive vessels from the mucous membrane of the nose, accessory sinuses of the nose, nasopharynx, Eustachian tubes and a portion of the tympanic cavity.

II. Two descending chains of glands on each side of the neck (lymphoglandular cervicales profundæ) shaped thus \wedge , like an inverted V. The apex of this group of glands lies just below the tip of the mastoid bone and under the sternomastoid muscle. One chain extends down the neck under the anterior border of the sternomastoid and is closely associated with the great vessels. The other group follows the posterior border of the sternomastoid and the anterior border of the trapezius, but is probably not directly connected with the supraclavicular groups of glands.^{15 16} This is an important anatomical feature, because a direct communication between these glands and the descending cervical chains would form a continuous line of lymphatics from the nose, pharynx, mouth and tonsils to the apex of the lungs.

What we wish to emphasize is that all of the six groups of glands previously mentioned drain into these descending chains; that there is a common point of origin and frequent anastomotic connections between the group along the great vessels and those in the posterior triangles; and that they all ultimately empty into the venous system—on the right side through the ductus lymphaticus dexter at the junction of the internal jugular and subclavian veins; on the left side through the thoracic duct.

In tuberculosis of the glands of the neck, we usually find both the anterior and the posterior groups involved. The statistics of pathologists and surgeons agree in finding, in a large majority of the cases of primary glandular infection, the oldest tubercular lesion in the glands around the anterior belly of the digastric and upper portion of the sternomastoid muscle.

Dowd,¹⁷ who has had the largest experience of any one in New York City with cases of this type, finds the oldest lesion in the so-called "*tonsillar gland*" at the angle of the jaw in 86

¹⁵ *Loc. cit.*

¹⁶ Bitze, H.: Ueber den Weg der Tuberkelbazillen von der Mund- und Rachenhöhle zu den Lungen, mit besonderer Berücksichtigung der Verhältnisse beim Kinde; Virchow's Arch. f. path. Anat. (etc.), 1906, CLXXXIV, 1-55.

¹⁷ Dowd, C. M.: The Surgical Treatment of Tubercular Cervical Lymph-nodes; Ann. Surg., 1905, XLII, 49-74.

per cent of his cases. Dowd also points out that in the majority of his patients, the onset is insidious; advice is sought because of rapidly enlarging glands; many patients give a history of frequent attacks of tonsillitis or pharyngitis; and a large proportion come in the late winter and early spring following the winter "colds."

Nicoll¹⁸ reports five hundred cases from Glasgow where tuberculous adenitis is a particularly common malady.

1. In nearly all the enlargement of the glands at the angle of the jaw was first noted.

2. He found evidence of the oldest lesion in the retropharyngeal glands.

3. In 70 per cent the glands were involved on both sides of the neck.

4. He observed, as we have also noted, that the size of the tuberculous glands increases and decreases with each attack of coryza or pharyngitis.

5. He thinks that the glands first enlarge as a result of pyogenic infection, and the tuberculous infection is secondary in the great majority of cases.

Wood in his experimental studies on the infection of the hog's tonsil with anthrax bacilli, comes to the opposite conclusion. He thinks the anthrax bacilli first penetrate the living, unaltered epithelium lining the crypts and by their multiplication devitalize the tissues and so pave the way for a secondary invasion.

Although it is often stated that miliary or pulmonary tuberculosis rarely results from a primary tuberculous cervical adenitis, statistics indicate a greater frequency. Von Noorden¹⁹ reports 149 cases of tuberculous cervical adenitis observed for a period of three years or more after operation. Twenty-eight died of pulmonary or generalized tuberculosis, and 14 others had a pulmonary lesion at the time of the last examination. Fischer,²⁰ in 1901, collected 1273 cases from the literature that had been observed from one to sixteen years after operation. His results are as follows:

Cured	57 per cent.
Local recurrence	28 per cent.
Died from tuberculosis.....	13 per cent.

Dowd²¹ concludes one of his articles with the statement that from 25 to 30 per cent of all cases of primary tuberculous cervical adenitis will develop tuberculosis elsewhere unless the glands are removed.

¹⁸ Nicoll: The Etiology and Treatment of Chronic Enlargement of Lymphatic Glands with Special Reference to Those of the Neck; Glasgow Med. Jour., 1896, XLV, 29-44.

¹⁹ von Noorden, W.: Über die operative Behandlung der Lymphdrüsen-Tuberkulose und deren Endresultate; auf Grund von 149 Fällen aus der Tübinger chirurg. Klinik; Beitr. z. klin. Chir., 1890, VI, 607-638.

²⁰ Fischer, F.: Krankheiten der Lymphgefäße, Lymphdrüsen und Blutgefäße; Deutsche Chir., 1901, Lief. 24a, p. 99.

²¹ Dowd: *Loc. cit.*

It has been shown by Park and Krumwiede²² that the majority of the tuberculous glands of the neck in children are due to an infection with the bovine bacillus.²³ This probably accounts for the better prognosis as regards a subsequent pulmonary infection in children. Karewski²⁴ reports 128 cases of primary tuberculous adenitis in children under 10 years of age, observed for from one to six years after operation. He found that only three had died of pulmonary or generalized tuberculosis. Von Behring for many years has contended that the bovine infections of childhood confer a certain degree of immunity against infection with the human tubercle bacillus in adult life. The incidence of bovine infection in children under four years of age is much greater in the British Isles than in Germany or Austria, but the death rate from pulmonary tuberculosis in Austria is nearly three times as great as in Great Britain.²⁵

There are, of course, many causes for an enlargement of the cervical glands aside from tuberculosis. The most common of these are:

1. Eczema, or any chronic infection or irritation of the scalp.
2. Pediculosis capitis. It is not infrequent in the out-patient department to see, both in children and adults, a marked enlargement of the posterior group of glands. The glands often enlarge rapidly, are tender; and the patients may appear quite ill. On several occasions, we have seen temperatures from 101 to 102.5° F., due solely to this condition. The glands will usually subside without suppuration if the pediculi are eliminated.
3. Acute attacks of tonsillitis or pharyngitis are always associated with more or less enlargement of the cervical glands. The degree of glandular reaction depends on the character of the infecting organism. In nasal and pharyngeal diphtheria and scarlet fever, the glandular reaction is marked; in Vincent's angina, there is a diffuse brawny infiltration of the tissues of the neck, and usually a suppuration in some of the glands along the great vessels, which necessitates external drainage. The ordinary tonsillitis causes an enlargement of the glands that usually subsides completely within three weeks or a month unless there is some chronic focus of infection in the tonsils, nasopharynx, sinuses or teeth. In some of the epidemic sore throats,^{26 27 28} due to a contamination of the milk supply with a particularly virulent strain of streptococcus, the characteristic features are the marked cervical adenitis and the severe constitutional symptoms. We have been able to observe for several years one of the Harvard

²² Park and Krumwiede: The Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis; J. Med. Research, 1910, XXIII, 205-368.

²³ Also refer to article by Ungermann: Untersuchungen ueber die tuberkulöse Infektion der Lymphdrüsen im Kindesalter; Tuberk. Arb. a. d. k. Gsndhtsamte., 1912, Heft 12, pp. 109-212.

²⁴ Karewski, F.: Die chirurgischen Krankheiten des Kindesalters; Stuttgart, 1894, p. 168.

²⁵ Fishberg: Pulmonary Tuberculosis, 1916. (Lea and Febiger.)

²⁶ Hamburger: The Baltimore Epidemic of Streptococcus or Septic Sore Throat and Its Relation to a Milk Supply; Johns Hopkins Hosp. Bull., 1913, XXIV, 1-11.

²⁷ Winslow: An Outbreak of Tonsillitis or Septic Sore Throat in Eastern Massachusetts and Its Relation to an Infected Milk Supply; J. Infect. Dis., 1912, X, 73-112.

²⁸ North, White and Avery: A Septic Sore Throat Epidemic in Cortland and Homer, N. Y.; J. Infect. Dis., 1914, XIV, 124-143.

students, infected during the Boston epidemic. He first came to Baltimore about six weeks after the subsidence of the constitutional symptoms. At this time, the glands at the angle of the jaw on the right side were markedly enlarged, hard, and matted together, but not adherent to the skin and not tender. We advised that nothing be done in an operative way. The following year he went to an Italian university for post-graduate work. The glands had much decreased in size, but following a coryza and mild sore throat, they rapidly enlarged and ruptured through the skin. This sinus continued to drain, and, following another coryza several months later, a second sinus appeared lower down. His Italian physician was sure he had tuberculous adenitis, and he again came to Baltimore for advice. A thorough physical examination, tuberculin tests and guinea-pig inoculation convinced us that the glands were not tuberculous. The tonsils and adenoids were removed, after which the sinuses healed and the glands gradually disappeared. At present, two years after the operation, there are no palpably enlarged glands, and at no time has there been any recurrence of the glandular swelling.

4. Carious teeth and alveolar infections. In this conditions, the submaxillary group of glands is chiefly involved. It is our opinion that caries alone, without infection of the gum or parodontal infection, will not cause any appreciable enlargement of the cervical glands.

5. Lues, Hodgkin's disease, the leukæmias and certain nutritional disturbances in children in which there is a general glandular enlargement.

6. Carcinoma or sarcoma. The earliest symptom of these growths in the tonsil or nasopharynx may be a rapid enlargement of the glands near the angle of the jaw.

A palpable enlargement of the upper cervical glands is an extremely common condition, particularly in children. Laser²⁹ examined 1216 school children:

137 had no enlargement of the cervical glands.

1079 had palpably enlarged cervical glands.

Volland³⁰ examined 2506 persons from seven to twenty-four years of age:

7 to 9 years of age—96 per cent had enlarged cervical glands.
 10 to 12 years of age—91 per cent had enlarged cervical glands.
 13 to 15 years of age—84 per cent had enlarged cervical glands.
 16 to 18 years of age—69 per cent had enlarged cervical glands.
 19 to 24 years of age—68 per cent had enlarged cervical glands.

Volland concludes that a large percentage of these cases have a latent tuberculous infection in their enlarged glands, which may become active and disseminated in later life.

Nicoll estimates that eighty per cent of the enlarged glands of the neck in the children of Glasgow are due to tuberculosis.

These statements must be received with reserve, however, since accurate information regarding the actual percentage of latent tuberculous infection in glands can be obtained only by the removal of a suspected gland and demonstration of the tubercle bacilli in the tissues by histological or cultural methods, or animal inoculation.

²⁹ Laser, H: Ueber die Häufigkeit des Vorkommens von tuberkulösen Halsdrüsen bei Kindern; Deutsche med. Wchnschr., 1896, XXII, 500-504.

³⁰ Volland: Ueber den Weg der Tuberkulose zu den Lungenspitzen, etc.; Ztschr. f. klin. Med., 1893, XXIII, 50-69.

B. FOCAL INFECTION³¹ WITH ESPECIAL REFERENCE TO THE TONSILS.

A focal infection may cause acute manifestations of a systemic intoxication, or it may be so insidious that months or years may elapse before general manifestations appear. The patient himself usually calls attention to the acute focal infection; and with proper and timely treatment the sequelæ, such as a general peritonitis from the appendix, a meningitis, cerebral abscess or general septicæmia from otitic infections, and perhaps a malignant endocarditis from tonsil infections, may be modified or entirely prevented.

It is the chronic focus of infection that in the end-result disables many thousands of people. A chronic focal infection may never give rise to local *symptoms*, but if searched for, the *signs* are as a rule quite evident. Although these insidious localized infections may be located in the abdominal organs, they are usually found in the genito-urinary tract, or in the upper air passages. Occasionally one is found in an unusual place. Dr. Frank Billings has reported two cases of arthritis in which the source was an infected ingrowing toe-nail.

The accessory nasal sinuses, tonsils, nasopharynx and teeth, are the most common situations in the upper air passages. There is clinical evidence, however, that a chronic mastoiditis may be of importance in the etiology, and certainly in the prognosis, of some of the general disorders of the digestive, cardio-vascular and renal systems.

It may be stated as a general law, that the focal infections that give rise to general systemic disorders are those with some mechanical obstruction of the natural channels of drainage. This has been true in our experience with nose and throat infections. In alveolar and tooth infections, it is usually the cases with infected pulp cavities that have been incompletely cleaned out and covered with a filling or crown that give rise to subsequent arthritic, anæmic or neurasthenic symptoms. Of the sinus infections, it is usually the cases in which there is enough obstruction to drainage to produce slight morning headaches that most frequently have some secondary manifestations of a general intoxication. We have, however, had a few very striking exceptions to this rule in sinusitis associated with arthritis.

The law mentioned above seems especially applicable to the tonsil. The majority of our cases with arthritic and renal lesions, in which the ultimate result was most satisfactory, have given a history of frequent attacks of tonsillitis during childhood; of one or more unusually severe tonsillitis attacks several weeks or months preceding the onset of their illness; or of a partial removal of their tonsils by operative measures or by means of the electric cautery. The end-result, as far

as the tonsil is concerned, is the same in each instance—the orifices of the crypts become partially occluded with scar tissue. A tonsillitis most frequently begins as an abscess in the lumen of the crypts, and under normal anatomical conditions, the contents of these crypts drain into the mouth. If the orifices of the crypts are partially occluded, however, the toxins and organisms more readily pass lateralward to the cervical lymph glands.

It is our opinion, as yet unproven by any large series of cases, that during the early stage of an acute tonsillitis there is a general bacteriæmia. This seems to be particularly true in patients with small, embedded tonsils and an abundance of scar tissue around the orifices of the crypts. If the organism happens to be of low virulence, or one to which there is a sufficient degree of immunity, it is quickly killed off, and there is no possibility of obtaining a positive blood culture except on the day that the general manifestations of the disease are at their height. If, on the other hand, it chances to be a viridans, or one of the streptococci that E. C. Rosenow has shown may have a specific affinity for certain organs, then serious metastatic infections occur.

It is possible that bacteria do not have a specific affinity for a given organ, but, as Billings has suggested, the local tissue conditions, supply of oxygen, etc., may be more favorable for the growth of the organism in one locality than in another. In malignant endocarditis, for example, *Streptococcus viridans* finds its way into the blood stream by one of the several possible portals of entry. This organism differs from other strains of streptococci in that it is less virulent and requires a high oxygen tension for its growth. Once in the blood stream, these organisms lodge in the capillaries of the heart valves,³² thrombi form and finally the characteristic vegetations. These vegetations furnish an excellent culture medium, and from them bacteria and occasionally infected emboli are liberated in the general circulation. It is probable that at the time of the primary infection, and at frequent intervals subsequently, the organisms lodge in capillary beds elsewhere, but the local conditions are not so favorable for their growth as they are in the heart valves. It must be remembered, however, that pneumococci, the pyogenic cocci and other organisms, may give rise to an endocarditis, and it is difficult to explain their selective location in the heart valves on the same theory.

However this may be, it is our experience that the patients with tonsils that have been damaged by previous infections, or partial operative procedures, are more prone to have some general disorder, following either an acute or chronic tonsillitis, than are those with approximately normal tonsils or with a first infection.

The tonsil is not the only portal of entry. Organisms probably pass through the mucous membrane of the nose, nasopharynx and pharynx more frequently than is generally supposed. We have, on several occasions seen, in patients

³¹ Refer to articles by: Billings, Frank: Forchheimer's Therapeutics of Internal Diseases, 1914, V, 169-181. Beck, J. C.: J. Am. Med. Assn., 1914, LXIII, 1636-1643. Ophüls, W.: J. Am. Med. Assn., 1915, LXV, 1719-1725. Articles in Vol. I, Kolle and Wassermann Handb. d. pathogen. Mikroorg., 2. Aufl., Jena, 1912. Zinsser, H.: Infection and Resistance, 1914, Macmillan Co. Barker, L. F.: The Treatment of Certain Chronic Infectious Processes, Brooklyn Med. J., 1906, XX, 345-351.

³² Refer to article by Bayne-Jones: Vascular Supply of the Heart Valves. To appear in the Anatomical Record.

whose tonsils and adenoids have been thoroughly removed, an enlargement of the glands of the neck, a return of arthritic symptoms, repeated attacks of rheumatic fever, and, especially frequently, a recurrence of chorea after a mild coryza or pharyngitis. It is possible that in these cases the specific organisms have remained latent in the cervical glands, and are activated and mobilized by the acute catarrhal process in the nose or pharynx. This undoubtedly occurs in tuberculous infections. A latent tuberculous focus in a gland or in the lung may become active and disseminated as a result of the hyperæmia occasioned by a neighboring catarrhal or pyogenic infection.

A chronic tonsillar infection may exist for an indefinite period without local symptoms, but we have found with few exceptions that the adjoining cervical lymph glands are enlarged and often slightly tender on palpation in these cases. This will be referred to later, for we regard the enlargement of the neighboring glands as one of the most important points in determining whether or not there is a chronic infection of the tonsil.

We have already referred to the experimental and post-mortem studies that show that particles of dust, granules of the aniline dyes and bacteria may pass through intact mucous membranes without damage to the tissues locally; and that lymph glands may contain tubercle bacilli and other organisms without histological or clinical evidence of their presence. It has been shown that tubercle bacilli may remain latent in a gland for long periods and finally produce general manifestations as a result of continued re-infection, or a decrease in the general resistance, due to fatigue, insufficient food or general unhygienic surroundings.

According to E. C. Rosenow and F. Billings, the joint, renal, muscular and valvular lesions secondary to a focal infection are due to bacterial thrombi. This means that the organisms get into the general circulation by way of the lymphatics. Clinical experience indicates that it is the toxins that are responsible for the joint symptoms in most of the arthritides. In gonorrheal arthritis, the organisms may usually be demonstrated in the joints, but in other forms the local cultures are almost invariably sterile. Many orthopedists believe that joint changes may be secondary to absorption from the gastro-intestinal tract, due to a ptosis or kink in the large bowel; and some entirely ignore the theory of focal infections.

Jackson,³³ in 1913, studied the joint reaction histologically at varying periods after an intravenous inoculation of rabbits with virulent streptococci. Two hours after intravenous administration, the organisms could be found in the capillaries of the periarticular tissues; intravascular collections of leucocytes were present after 10 hours, and after 24 hours an exudation and migration of leucocytes into the joint cavity had occurred.

Animal experiments, such as the intravenous injection of living organisms in rabbits, do not necessarily, in our experience, reproduce the clinical conditions. We have found that

joint or periarticular suppuration will result in about 50 per cent of the animals injected. This is true when the streptococci injected are obtained from a focal lesion in an arthritis case, the throat in scarlet fever, the urine, an empyema or an accessory nasal sinus infection. Furthermore, these organisms may produce joint lesions in some rabbits, but fail to have any effect on others. Frequently, streptococci isolated in pure culture from a focal infection in a patient with multiple arthritis may fail to produce any joint lesion in rabbits, even though the subsequent clinical course of the patient would indicate that this organism was responsible for the arthritic symptoms. In other words, the reaction of the tissues—chemical, immunological or circulatory—is more important in determining the location of an infection than is the specific affinity of a given organism for certain organs.

Faber,³⁴ from his experimental work in 1915, has concluded that the synovial membrane of a rabbit's joint may be *sensitized* by either of the following methods:

1. By repeated intravenous injections of streptococci of attenuated virulence.
2. By injecting into the joint cavity a suspension of killed streptococci. After all local reaction has disappeared, intravenous injections of minute doses of living streptococci of the same strain will give rise to a definite arthritis in the joint previously sensitized.

After a rabbit's joints are once sensitized by either of these methods, an arthritis may develop following the intravenous administration of doses so small that in a normal animal no symptoms whatever would result. The joint reaction may not occur, however, if any other organism, such as the pneumococcus, staphylococcus or *B. typhosus* is used, either for sensitizing the joint or for the subsequent intravenous injection. The organism used must be a streptococcus and the same strain must always be employed in both the joint and the intravenous injections.

Faber's conception of the etiology of a relapsing arthritis is that it is due to the effect of a virus upon a homologously sensitized joint. This theory might explain the frequent recurrence of arthritis after an attack of rheumatic fever; also some of the more chronic forms of arthritis with a small focus of infection in a tooth, tonsil, accessory nasal sinus, prostate, etc.

The one great principle in the therapy of systemic diseases secondary to a focal infection is a thorough removal of the primary focus. An infected tooth in a patient with arthritis is probably best treated by extraction; an infected accessory nasal sinus should be well drained, and, in many instances, the chronically infected mucosa lining the sinus should also be removed; radical surgical procedures should be resorted to, if necessary, to control a chronic otorrhea.

A partial tonsillectomy, due to the obstruction of the crypts of the remaining portion by scar tissue, may transform a re-

³³ Jackson, L.: Experimental Streptococcal Arthritis in Rabbits; Jour. Infect. Dis., 1913, XII, 364-385.

³⁴ Faber, H. K.: Experimental Arthritis in the Rabbit. A Contribution to the Pathogeny of Arthritis in Rheumatic Fever; J. Exper. Med., 1915, XXII, 615-628.

latively harmless hypertrophied tonsil into one that subsequently gives rise to the most serious general disorders.

A tonsillectomy, properly done, is really a major surgical procedure, and should not be undertaken unless the operator is thoroughly familiar with the principles and practice of the general rules of surgery. Three of the most important rules of surgery are absolute cleanliness, protection of the tissues against needless injury, and control of hemorrhage. It is unfamiliarity with the methods of controlling bleeding that is responsible for the incomplete tonsillectomies and many of the post-operative complications. This will be referred to later. Serious bleeding not infrequently occurs and occasionally with a fatal result. One of us once heard a prominent laryngologist reassure a patient with a post-operative hemorrhage by telling him that the bleeding would surely stop when his blood-pressure became low enough.

In addition to removal of the primary focus of infection, other therapeutic measures are of great importance in the treatment of these patients with some general disorder secondary to a focal infection. It must be remembered that metastatic infections in the adjoining lymph glands may remain after the removal of the original focus. Every effort should be made to maintain the natural defences of the body. All exhausting and depressing measures, such as an insufficient diet, mental or physical fatigue, and frequent hot baths, should be avoided. Rest, good food, fresh air and sunshine are the essentials. They are purposely mentioned in this order to emphasize the importance of rest.

Other measures might be mentioned, such as the hyperæmia obtained by baking, in joint affections; the use of drugs, and, finally, the use of vaccines. The use of stock vaccines is unscientific and often dangerous. Autogenous vaccines in the chronic forms of arthritis and myositis have seemed to possess some value, but the good result in the management of these cases is due more largely to improvement in health by hygienic measures (Billings). This is just as true of the treatment by vaccines of chronic sinus and ear infections as it is for arthritis.

Summary.—Focal infections may give rise to acute rheumatic fever, simple and malignant endocarditis, septicæmias due to various organisms, some types of arthritis, myositis and nephritis, neuritis, arteriosclerosis, general debility, and a great variety of nervous disorders designated as neurasthenia.

Focal infections may occur anywhere in the body, but are perhaps more frequent in the accessory nasal sinuses, tonsils, teeth, gums, and genito-urinary tract.

Neighboring glands become secondarily infected and may harbor the organisms and continue to infect the blood-stream after the removal of the original focus. On this account general measures in the treatment of systemic diseases secondary to focal infections are of great importance.

Organisms entering the blood-stream by way of a focal infection may have a specific affinity for the endocardium, the synovial membranes, the blood-forming organs, the muscles or the kidneys. On the other hand, the selection of the organ

involved may be due to the local chemical, mechanical or circulatory conditions.

As a general rule, the focal infections that are most likely to give rise to secondary disorders elsewhere in the body are those in which there exists some obstruction to the natural channels of drainage.

A chronic tonsillitis may be defined as a condition of the tonsils in which there is an increase of fibrous tissue, adhesions between the tonsil and pillars, or some other evidence of an inflammatory reaction together with a palpable enlargement of the deep cervical glands at the angle of the jaws.

A chronic tonsillitis may result from frequent acute attacks, or from a long continued sub-acute inflammatory process secondary to pyorrhea, caries of the teeth, obstructed nasal passages, or chronic infection of the accessory nasal sinuses or ears. In each of these conditions, the tonsils are more or less constantly bathed with irritating discharges. When searching for a focus of infection, one must not forget that the evident chronic tonsillitis may be *secondary* to one of the above-mentioned conditions. In such cases the removal of the tonsils without attention to the nose, sinuses, ears, or condition of the teeth, may give very disappointing results. The patient may continue to have attacks of pharyngitis with swelling of the cervical glands, or inflammatory conditions of the larynx and bronchi that were never present before the operation. In this respect, the tonsils and adenoids apparently protect the lower air passages.

From the standpoint of the treatment of an infectious arthritis or a glomerulo-nephritis, the removal of chronically infected tonsils, leaving infected teeth or sinuses, may be of no benefit, but an actual injury to the patient. In the first place, the surgical procedure is quite a shock to such patients, and most important is the fact that organisms in the discharge from the sinuses, teeth, etc., may continue to pass through the mucous membrane of the pharynx to the cervical lymph glands.

In every case where a tonsillectomy is contemplated, it must first be determined whether the tonsil infection is localized or is secondary to some chronic infection in the mouth or upper air passages. If the nasal passages and teeth are normal, a removal of the tonsils and adenoids alone is indicated. If, however, there is any marked nasal obstruction, sinus infection, alveolar abscess, or extensive pyorrhea, these conditions should first be remedied before the operation on the tonsils is undertaken.

These precautions not only insure a relatively clear field for the tonsil operation, but the ultimate results of the tonsillectomy will be more favorable in any large series of cases.

C. PORTALS OF ENTRY OF TUBERCLE BACILLI.³⁵

There are two main pathways by which the tubercle bacillus gains entrance to the body; one is by direct inhalation and the other by ingestion. Trauma is a third and relatively

³⁵ Bacmeister, A.: Wesen und Gang der tuberkulösen Infektion bei Entstehung der menschlichen Lungenphthise; *Ergebn. d. inn. Med. u. Kinderh.*; Berl., 1913, XII, 515-552.

infrequent cause of infection with the tubercle bacillus. There are many cases on record, however, of tuberculous infection in the children of Russian Jews that date from the religious ceremony of circumcision.

Direct Inhalation.—There is considerable evidence against the view that the inhalation of tubercle bacilli is the most common mode of infection.

1. The dust on the street contains very few living tubercle bacilli. It is generally believed by tuberculosis experts that no one ever contracts this disease out-of-doors. As long as the sputum is moist, the bacteria cannot be blown about, and they are rapidly destroyed by the process of drying, by exposure to sunlight, dilution by rains, etc. The dust raised in houses by the various cleaning processes, however, often does contain virulent organisms, as was shown by Cornet and others. Virulent bacilli may be found in hallways and dark corners of rooms for months after their introduction.

2. The bacteriological examinations of the smaller bronchi that have been made in persons meeting an accidental death, and by means of the bronchoscope in normal persons, all show that the lower air passages are for the most part sterile.

This is probably due to the various protective mechanisms—the mucous membrane of the nose, the lymphoid tissue in the throat, the abundant secretion of mucus in the upper air passages, and the ciliated cells of the trachea.

3. The tubercle bacillus is protected by a very resistant, waxy capsule, and may therefore be analogous to a particle of dust. It is difficult, however, on the inhalation theory to explain why the bacilli should find their way to and set up the diseased process almost invariably in the apex of the lung, whereas the organisms that find their way to the basal portion of the lungs are destroyed or in some way prevented from forming primary tubercles in this situation.

Ingestion.—This term includes the passage of organisms through the mucous membrane of the entire digestive tract, from the lips to the rectum.

A most important fact is that the tubercle bacilli may pass through normal skin and mucous membrane without leaving any gross or microscopical evidence of their presence. These tubercle bacilli may lodge in the glands draining the area of their portal of entry and set up a diseased process locally; may remain latent in the glands for long periods without clinical evidence of their presence; or, finally, may pass through a series of glands with or without causing local disease, and thus enter the blood stream.

The healed or arrested tuberculous process so frequently found at autopsy in the glands of the neck, at the root of the lungs, or in the mesentery, means that the organisms have gained entrance by way of the throat, the mucous membrane of the trachea or bronchi, or through the walls of the intestine. Other organisms, such as the cocci, undoubtedly gain entrance by the same channels, but not being endowed with the waxy capsule and resistant properties of the tubercle bacillus, they are, for the most part, promptly killed by the body fluids.

In the experimental infection of guinea-pigs by the inhalation method, where the head of the animal is confined in a

tube and enormous numbers of virulent bacilli inspired, as much, if not more, tuberculosis is found in the cervical, peribronchial and mesenteric glands as in the lungs.

The infection of children with tuberculosis is probably for the most part by ingestion. It has been shown by Park and Krumwiede that the bovine bacillus is responsible for 61 per cent of the tuberculous glands of the neck in children under five years of age. The infection in these children must be due entirely to the ingestion of infected food, and the passage of organisms through the mucous membrane or lymphoid elements of the throat. It is fortunate that the bovine bacillus rarely produces pulmonary lesions (only four cases of pure bovine infection were found in the 831 cases of pulmonary tuberculosis examined by Park and Krumwiede) for, otherwise, infant mortality from tuberculosis would be enormously increased. There is evidence that the bovine infection of childhood tends to immunize them against a subsequent infection with the human bacillus.

The incidence of bovine infection becomes less frequent as the age increases. (Park and Krumwiede.)

1. In 39 cases of tuberculous cervical adenitis in children under 5 years of age, the human bacillus was the predominating organism in 15, and the bovine bacillus in 22.

2. In 58 cases of cervical adenitis in children from 5 to 16 years of age, 36 were due to the human, and 22 to the bovine bacillus.

3. In 37 cases of cervical adenitis in adults, 36 were due to the human and 1 to the bovine.

The infection of children with the human bacillus is largely due to the fact that for the first six or seven years of its life, the average child spends the greater part of each day on the floor, and its soiled hands and toys are frequently in its mouth.

In the house where a tuberculous person resides, the floors become infected by coughing and careless expectoration; but the real tragedy is the infection of children in this way in houses where there has been no tuberculosis. Infection of the floors in such houses is due to the carrying in of virulent tubercle bacilli on the shoes. It is in this way, rather than through dust infection, that expectoration on the sidewalks or in public conveyances becomes a serious factor in the spread of the disease.

The seriousness of careless expectoration on the street or in public places might be more fully appreciated if the public realized that in the great majority of persons with tuberculous infections of all kinds, the principal lesion is in the lungs. In Germany, it has been estimated that eleven-twelfths of all the cases of tuberculosis of all ages have a pulmonary lesion. This means that practically every case of tuberculosis has at some time tubercle bacilli in the sputum, and carelessness in disposing of the excreta at this period may lead to the infection of many others, particularly children.

Tuberculosis of the Tonsils and Adenoids.—We purposely speak of this group of 46 cases as “apparently primary tuberculosis” of the tonsils and adenoids, for we realize fully that the incompleteness of our data would not justify any dogmatic

statement as to whether or not the tonsillar lesion was the only tuberculous focus in the body.

As to the incidence of focal tuberculous lesions in the body, von Behring³⁶ states that Naegeli of Zurich, in a series of post-mortem examinations made for the purpose of establishing the importance of Koch's bacillus, found:

1. Infants under 1 year of age failed to show any focal lesion.
2. From 1 to 5 years of age 17% had some focal tuberculous lesion.
3. From 5 to 14 years of age 33% had some focal tuberculous lesion.
4. From 14 to 18 years of age 50% had some focal tuberculous lesion.
5. From 18 to 30 years of age 96% had some focal tuberculous lesion.
6. After 30 years of age, every body coming to autopsy has some evidence of an infection with the tubercle bacillus.

These amazing statistics have been confirmed in practically all the thickly populated centers of the world.

There are two methods of making a diagnosis of a focal tuberculous lesion with absolute certainty: one is the finding of the bacilli of Koch in the diseased process by microscopic examination or demonstrating their presence by animal inoculation; and the other is by the reaction of the patient to tuberculin.

In our series of cases with focal tuberculous lesions, neither of these diagnostic procedures has been carried out systematically. The diagnosis of a tuberculous process in the tonsil or adenoids in our cases is based on the presence of microscopical tubercles. In 24 cases there was characteristic caseation. The diagnosis of tubercles in tonsils where there is no caseation is based on the local collection of so-called epithelioid cells, with the characteristic flattening of the peripheral cells and a surrounding collection of small lymphocytes. Foreign-body giant-cells occur not infrequently in the tonsils, but we have carefully excluded all cases from this series in which there was some doubt as to whether the lesion was due to a foreign-body reaction, or to the tubercle bacillus.

In regard to the tuberculin test, it has been definitely established that a positive reaction never occurs unless there is an anatomical tubercle in the body. An enormous intravenous dose of tuberculin may be given a normal animal without the slightest effect; whereas a relatively small amount of tuberculin will cause a violent reaction or promptly kill an animal with a small, localized tuberculous lesion.

A large percentage of children beyond the second year, and practically every adult, will give a positive tuberculin reaction. "Tubercular infection, however, is far from meaning tubercular consumption." Whether the entrance of tubercle bacilli into the body becomes harmful or not, depends upon several factors. According to Dr. Trudeau, "Tuberculosis attacks

the weak, cancer the strong."³⁷ By "the strong," he means the person whose tissues tend to proliferate actively when subjected to any bacterial or mechanical irritation; and by "the weak," those persons whose tissues do not react promptly or energetically to such stimuli.

The degree of virulence of the infecting organism is another important factor. In the Saranac laboratory there is a strain of the tubercle bacillus that has almost completely lost its virulence as a result of many years of cultivation on artificial media. Even large doses will not produce visceral lesions in guinea-pigs, although they produce the characteristic caseating lesions in the lymph glands.

In focal tuberculous lesions, particularly in the cervical glands, the quantity of the infecting bacilli and whether we have to do with a single infection or oft-repeated infections over a long period, are factors of greater importance. Thus a primary tuberculous infection of the tonsils or adenoids may be responsible for a recurring tuberculous cervical adenitis.

A histological tubercle is a non-vascular structure that is nourished by a process of osmosis and diffusion. Any acute catarrhal or pyogenic inflammation in the neighborhood of a tuberculous lesion, even though the latter has long been latent, may seriously alter the prognosis. The hyperæmia associated with such inflammatory conditions results in an increased absorption of the poisons made by the tubercle bacilli, and the lassitude, slight evening rise of temperature and loss of appetite so frequently seen after a spring "cold" may often be explained in this way. But what is more serious is that the tubercle bacilli themselves may escape from a latent focus at such times and result in a widespread dissemination of the disease.

It has been pointed out previously that anatomical and experimental evidence indicates that in all the infections of the upper cervical glands, with the exception of the relatively rare retrograde infections, the organisms gain entrance through the mucosa or lymphoid tissue of the nose, throat and mouth. Dowd has called attention to the fact that a large proportion of patients with tuberculous adenitis first apply for medical advice after a "cold." Is it not possible that the majority of these patients have a primary lesion in the tonsils or adenoids, and even though the affected cervical glands are removed, the recurrence and subsequent dissemination of the disease may to a large extent be due to the neglected throat infection?

There are but few statistical studies on which to base an answer to this question. We know of no publication on the relation of tuberculosis of the tonsil and adenoids to cervical adenitis that is based on a thorough scientific study of the throat and glandular conditions. It is certain that the routine histological examination in each case of a few sections of the tonsils and adenoids removed at operation will fail to disclose the true incidence of tuberculous infections in these tissues. We have had 23 cases of tuberculous adenitis, proved by re-

³⁶ von Behring, E.: Über Lungenschwindsuchtentstehung und Tuberkulosebekämpfung; Deutsche med. Wchnschr., 1903, XXIX, 689-697.

³⁷ These same words will be found among the conclusions of Dr. Maud Slye's article on the Incidence and Inheritability of Spontaneous Cancer in Mice; Jour. Med. Research, 1915, XXXII, 159-200.

moval and microscopical examination of a gland, in which no clinical or histological evidence of tuberculosis was found in the tonsils or adenoids removed at operation. This does not necessarily mean that the lymphoid tissue in the throat was not infected. In none of these 23 cases were the tonsils and adenoids stained for tubercle bacilli; no attempt was made to cultivate the tubercle bacilli from the tissues, and animals were not inoculated. The routine histological examination we refer to consists of a study of only four or five sections of the tonsils and adenoids from each case, and therefore focal tuberculous lesions might easily be overlooked.

The great majority of the cases with tuberculous cervical adenitis are operated on by a general surgeon who ignores the nose and throat condition and soon loses sight of his patients.

We have already referred to the observations of von Noorden on 149 cases of primary tuberculous adenitis observed for a period of three years or more after the operation on their glands; 28 had died of pulmonary tuberculosis, and 14 others had symptoms of a pulmonary infection. Fischer collected from the literature 1273 cases that had been observed from one to sixteen years after operation on their glands; reported cured 57 per cent; local recurrence in 21 per cent; died from pulmonary tuberculosis 13 per cent. It cannot be denied that in a certain proportion of these cases the patient probably had a pulmonary lesion and tubercle bacilli in the sputum at the time of the operation, and the glandular infection was secondary. Others may have had an arrested pulmonary lesion that was activated by the anesthetic; but in a large group the portal of entry is in the throat, and the primary lesion, if searched for, will probably be found in either the tonsils or the adenoids. Bartel and Spieler²⁸ have found that 11 per cent of the animals inoculated with tonsils developed tuberculosis; yet in no instance did they find histological or gross tuberculous lesions in the tonsils used for the inoculations. Harbitz also obtained positive inoculation results with tonsils and cervical glands that showed no microscopical tuberculous lesions.

In view of these facts and the anatomical relation of the lymphoid structures in the throat to the cervical glands, it would seem to us that the tonsils and adenoids should be removed whenever there is any hyperplasia of the cervical glands that is not due to lues, new growth, or any of the blood diseases. We would also exclude the group especially frequent in children, where the hyperplasia of the cervical glands is a part of a general glandular enlargement.

Of a total of 1000 tonsillectomies at The Johns Hopkins Hospital in which the tonsils and adenoids have been examined histologically:

139 were from colored patients, and of these 11, or 7.9 per cent, were tuberculous.

861 were from white patients, and of these 35, or 4 per cent were tuberculous.

²⁸ Bartel, J. and Spieler, F.: *Experimentaluntersuchungen über natürliche Infektionsgelegenheit mit Tuberkulose*; Wien. klin. Wchnschr., 1907, XX, 1144-1150.

Age Incidence of those with Tuberculous Lesions of the Tonsils or Adenoids.—The youngest patient was 4, the oldest 34 years of age.

1. Between the ages of 4 and 5 there are 5 cases: Tuberculous lesions were found in the tonsils alone in 4 cases; in the adenoids alone in 1 case.

2. Between the ages of 5 and 10 there are 14 cases: Tuberculous lesions were found in the tonsils alone in 9 cases; in the adenoids alone in 5 cases.

3. Between the ages of 11 and 15 there are 10 cases: Tuberculous lesions were found in the tonsils alone in 6 cases; in the adenoids alone in 4 cases.

4. Between the ages of 16 and 25 there are 13 cases: Tuberculous lesions were found in the tonsils alone in 7 cases; in the adenoids alone in 3 cases; in both the tonsils and adenoids in 3 cases.

5. In those over 26 years of age there are 4 cases: Tuberculous lesions were found in the tonsils alone in 3 cases; in the adenoids alone in 1 case.

In 23 of the 46 cases with a tuberculous lesion in either the tonsils or the adenoids the size of the deep cervical glands at the angle of the jaw, the periadenitis and the history all suggest a tuberculous cervical adenitis.

In 20 of these 23 cases with clinically tuberculous glands of the neck, there was a history of frequent attacks of tonsillitis.

Clinical Symptoms.—In 40 of the 46 cases, there was a history of frequent attacks of tonsillitis.

In 43, the deep cervical glands at the angle of the jaws were palpably enlarged. In 23 of these cases, there was a periadenitis, suggesting tuberculous glands.

In five, an unexplained elevation of temperature had been noted for several weeks before their admission to the hospital.

In four, the tonsils were removed on account of an arthritis of the infectious type. In this group particularly, there was no suspicion of a tuberculous lesion until the routine histological examination of the tonsils.

In one, the tonsils were removed on account of blood and albumin in the urine—a glomerulo-nephritis.

In one, the tonsils and adenoids were removed on account of a tuberculous iritis. In this case, tubercles were found in the adenoids alone.

Clinical Appearance of the Tuberculous Tonsils.—It was impossible in any of these cases to foretell from the appearance of the tonsil whether or not it contained a tuberculous focus. Even after the tonsil had been removed and sectioned, we were never able on macroscopic examination to differentiate with any certainty a tuberculous lesion from a chronic inflammatory reaction with detritus in the crypts. On microscopic examination, a collection of detritus in a crypt or an area of hyaline degeneration with foreign body giant cells may closely simulate a tuberculous process.

The tonsil and pharyngeal lesions so frequently seen in advanced cases of pulmonary tuberculosis, are always asso-

CHART I.—TUBERCULOSIS OF TONSILS OR ADENOIDS. ABSTRACT OF CASES IN TABLE I.

Age 1 to 5 years.

No. of case.	Age.	Condition at time of operation.						Condition at present time.				
		Family history of Tbc.	Cond. lungs at time of operation.	Size of tonsils and adenoids.	Size cervical glands time of operation.	Tbc. test time of operation.	Length of time observed since operation.	General health.	Cervical glands.	Tuberculin test.	Condition of throat.	Remarks.
1	4	B. has Tbc. tonsils.	Normal.	Large.	Hickory-nuts.	—	4½ years.	Good.	Not palpable.	—	Normal.	Lungs normal. No symptoms of Tbc.
2	5	None.	"	Very large.	5×8 cm. on left.	—	3 years.	"	"	—	"	Lungs normal. No symptoms of Tbc.
3	4	—	"	Large.	6×2 cm. on right.	Pirquet +	3 years.	"	"	Pirquet +	"	Lungs normal. No symptoms of Tbc.
4	5	None.	"	"	5×3 cm. on right.	Pirquet +	2 years.	"	1×2 cm. on right.	—	"	Lungs normal. Glands suppured; treated by local incision; sinus closed. Temperature normal.
5	5	—	Dullness at apices; no râles.	Small.	Large; especially on right.	Pirquet +	2½ years.	"	Smaller.	Pirquet +	"	Lungs as before; X-ray shows mediastinitis.

Age 6 to 10 years.

6	8	None.	Dullness at both apices.	Very large.	Enlarged on both sides.	Pirquet +	3½ years.	Good.	No glands on right; small on left.	Pirquet + Calmette 1%+	Normal.	Lungs as before.
7	10	"	Normal.	Large.	Not palpable.	—	3 years.	"	Not palpable.	—	"	" normal.
8	9	"	"	Very large.	Enlarged; matted.	Pirquet +	3 years.	"	" "	Pirquet. ?	"	" "
9	9	"	"	" "	2×3 cm.	Pirquet +	2 years.	—	1½×1 cm.	Pirquet +	"	" "
10	10	"	"	Enlarged; especially right.	2×3 cm.	—	1½ years.	—	1.5×3 cm.	Pirquet +	"	" " ; glands on left suppured.
11	10	"	"	Very large.	Enlarged on both sides.	—	2½ years.	Good.	½ cm.	Pirquet +	"	Lungs normal.
12	7	—	"	" "	Enlarged on both sides.	Pirquet +	2 years.	"	Smaller.	Pirquet +	"	" "
13	7	None.	"	Large.	Enlarged on both sides.	—	1½ years.	"	"	—	"	" "
14	7	"	"	"	4×3 cm. on right; enlarged on left.	Pirquet +	1 year.	Improved.	Glands on R. removed; smaller on left.	—	"
15	8	"	"	Very large.	6×4 cm. on left; 2×3 cm. on right.	—	Died. Tbc. meningitis.
16	10	Mother and grand-mother.	"	Enlarged; especially on left.	Enlarged.	Pirquet +	1 year.	Improved.	Smaller.	Pirquet +	Normal.	Lungs normal.
17	10	—	"	Very large.	1 cm. both sides.	—	9 months.	Good.	"	Pirquet +	"	" "
18	10	None.	"	Enlarged.	4×8 cm. on left.	Pirquet +	1½ years.	"	Not palpable.	—	—	—

Age 11 to 15 years.

19	14	None.	Normal.	Very large, especially right.	6×10 cm. on left; palpable on right; incised on left.	—	3½ years.	Good.	Palpable.	—	Normal.	Lungs normal.
20	9	—	"	Large; especially left.	7×5 cm. on left. Incised.	—	3½ years.	"	—	—	—	—
21	11	None.	"	Partially removed.	8×10 cm. on left; slightly enlarged on right.	Pirquet +	2½ years.	"	Pirquet +	Normal.	Lungs normal; glands on left suppured; incised; healed.
22	14	"	"	Very large.	5×7 cm. on left; palpable on right.	Calmette +	8 months.	Improved.	Glands larger.	—	"	Lungs normal.
23	13	"	"	" "	6×4 cm. on right; incised; palpable on left.	Pirquet +	1 year.	Good.	Smaller.	Pirquet +	"	" "
24	12	—	"	Not enlarged.	5×3 cm. on both sides.	—	9 months.	"	1×2 cm.	—	"	" "
25	15	—	"	Partially removed.	Enlarged both sides; incised on right.	Pirquet + Calmette +	1½ years.	"	Smaller.	Pirquet +	"	Lungs: impaired percussion note at both apices.
26	12	—	"	Partially removed.	Slightly enlarged.	—	1½ years.	"	"	Pirquet +	"	—
27	14	—	"	Small.	1½ cm. both sides.	—	1 year.	"	"	—	"	Lungs normal.
28	13	—	"	Enlarged.	2×3 cm. both sides.	—	9 months.	"	Smaller on right; same on left.	Pirquet +	"	" "
29	11	—	"	Very large.	2 cm. both sides.	Pirquet + Calmette 1% 0.	9 months.	Not improved.	Recurrence tbc. glands.	—	—	Lungs: suspicious involvement of right apex.

CHART I.—Continued.

Age 16 to 25 years.

Condition at time of operation.								Condition at present time.				
No. of case.	Age.	Family history of Tbc.	Cond. lungs at time of operation.	Size of tonsils and adenoids.	Size cervical glands time of operation.	Tbc. test time of operation.	Length of time observed since operation.	General health.	Cervical glands.	Tuberculin test.	Condition of throat.	Remarks.
30	19	—	Imp. of left apex & râles.	Large, especially left.	Enlarged.	—	3 years.	Good.	Not palpable.	—	Normal.	—
31	18	—	Normal.	Enlarged.	“	—	2½ years.	“	None on right, ½ cm. on left.	—	“	Lungs normal.
32	25	Grandfather died pul. Tbc.	“	“	Enlarged, especially on right.	—	1½ years.	“	—	—	—	—
33	20	None.	“	Very large. R. large; L. small.	Not enlarged.	—	2½ years.	“	Not enlarged.	—	Normal.	—
34	18	“	“	“	“	—	3 years.	Not improved.	Not enlarged.	—	—	—
35	19	“	Imp. at R. apex.	Not large	3×8 cm. on left sinus.	Calmette 1%.	2½ years.	Good.	Sinus healed in 6 months.	—	—	Lungs normal. Sinus reopened in 2½ years; glands excised.
36	24	“	Normal.	“	None palpable.	—	2 years.	“	Not enlarged.	—	—	Lungs normal.
37	22	“	“	“	5×8 cm. on right; incised.	—	2 years.	—	Recurrence on R.; enlarged on left.	—	Normal.	Lungs: pleurisy 1½ years after operation.
38	19	“	“	R. larger than left.	5×8 cm. on right; enlarged on left.	—	9 months.	Good.	2×3 cm. on right; not palpable on left.	—	“	Lungs normal.
39	23	“	“	Small.	Large mass on right; enlarged on left.	Calmette 1%.	9 months.	—	Discharging sinus on right.	—	“	Lungs: slight impairment at right apex; with râles.
40	18	—	“	Slightly enlarged.	None palpable.	—	6 months.	Improved.	Not enlarged.	—	“	Lungs normal.
41	10	None.	Thickened pleura.	R. larger than left.	6×4 cm. on left.	Calmette 1% 0 5% doubtful.	9 months.	Poor.	Sinus above left clavicle.	—	—	Lungs: evidence of active Tbc. at left apex.
42	22	—	Normal.	R. larger than left.	1×2 cm. both sides.	—	8 months.	Good.	Smaller.	Pirquet +	—	Lungs normal.

Over 26 years of age.

43	29	Mother died pul. Tbc.	Imp. at R. base.	Enlarged.	Mass on both sides; incised on left.	Pirquet +	3 years.	—	Mass palpable on L., slightly enlarged on right.	—	—	—
44	27	None.	Normal.	Not enlarged.	2×3 cm. both sides.	Pirquet + Calmette +	2½ years.	Well for 2 years.	After 2 years caseous glands removed on R.	Pirquet +	Normal.	Lungs: Imp. at right apex; with râles.
45	31	“	“	L. larger than R.	None palpable.	—	2 years.	Good.	Not enlarged.	—	“	Lungs normal.
46	34	“	“	Slightly enlarged.	3×2 cm. both sides.	—	2 years.	Well for 1 year.	Palpable.	—	“	Lungs: definite pulmonary Tbc. developed after 2 years.

ciated with superficial ulcerations.³⁹ In these “apparently primary” tuberculous lesions of the tonsils, however, we have never seen a superficial lesion.

The tonsils were hypertrophied in 34 of our 46 cases. In nine, they were small, inconspicuous, and densely adherent to the anterior and posterior pillars. In 3 instances, the patients gave a history of a partial removal of their tonsils from one to five years previously.

In five cases in which a tuberculous lesion was found in only one tonsil, the tuberculous tonsil was definitely larger than the one on the opposite side. The increase in size of the tonsil in these cases was due to a hyperplasia of the mononuclear elements, and the germinal centers were unusually large and prominent.

³⁹ Tubercle bacilli never produce a lesion that begins on the surface of mucous membranes, with the possible exception of lupus. In the secondary ulceration of the pharynx, in the larynx and intestines, the bacilli first penetrate to the submucous layer. The disease process may eventually cause ulceration of the overlying mucous membrane. This probably accounts for the characteristic undermining of tuberculous ulcers.

The tuberculous focus in the tonsils was found most frequently near the capsular surface at the bottom of the crypts. In many instances, the tonsils and adenoids that contained a tuberculous focus were hyperplastic, and showed but little microscopical evidence of a chronic inflammatory process.

We have already emphasized the fact that the tuberculous lesion in the tonsils and adenoids in these cases was discovered during the routine histological examination. Many tuberculous lesions were probably missed. Our object, however, is not to determine the incidence of such lesions but to follow up the cases we have and note the ultimate outcome.

We shall not take up further time or space in summarizing these 46 cases, as they are all given in some detail in the following chart.

From the point of view of the operation, it is worthy of note that ether anæsthesia was used in every case. There were no immediate complications of any kind, and so far as we can determine no ill effects due to the operation have subsequently developed in any of the 46 patients. One patient had an attack of pleurisy nearly two years after the operation, and in others it was necessary subsequently to remove tuberculous

glands of the neck. There is no evidence, however, that the operation has in any case made the condition of the glands worse or caused a latent pulmonary lesion to become active.

It is also worthy of note that in every case the operative wound in the throat healed as readily as in the non-tuberculous patients. The hyperlastic pharyngitis noted in the subsequent examination of these cases is also present in a large percentage of all our tonsil cases, as may be seen by referring to the detailed tables of the other groups.

In each case a parent, or the family physician, was notified as soon as the tuberculous lesion in the tonsil or adenoid was discovered, and every effort was made to have the patients treated as though they were tuberculous. The Phipps Dispensary for the Treatment of Tuberculosis has co-operated, and in many instances of tuberculous cervical adenitis very striking results were obtained by tuberculin and general hygienic measures. We were also greatly aided by Dr. E. A. Park and others of the Harriet Lane Home for Invalid Children.

D. THE INDICATIONS AND CONTRA-INDICATIONS FOR TONSILLECTOMY.

Indications for Tonsillectomy.

I. *Local disorders in the upper air passages:*

1. Hyperplasia of the tonsils causing difficulty in swallowing, articulation or breathing. One should always bear in mind the possibility of a "status lymphaticus."

2. Frequent tonsillitis or quinsy. In these cases a careful examination must be made of the teeth, accessory nasal sinuses, nose and ears. Infection in any one of these situations may be primarily responsible for the frequent tonsil attacks.

3. A chronic laryngitis or bronchitis may often be benefited by a nose or throat operation.

4. A chronic catarrhal or suppurative otitis media or an Eustachian tube affection.

5. Chronic diphtheria carriers. Some of these cases will clear up after removal of the tonsils and adenoids. Often a pure culture of the Klebs-Löffler bacillus, virulent for guinea-pigs, may be obtained from the bottom of the crypts of the excised tonsils in cases that have no clinical manifestation of their presence.

6. Any of the various "reflex neuroses" in children; such as asthma, paroxysmal nocturnal attacks of coughing, enuresis nocturna, and sometimes convulsive seizures resembling petit mal. These are sometimes due to tonsillar or nasopharyngeal disease.

7. New growth. The carcinomas are best treated by operative measures. The sarcomas, however, usually respond promptly to radium treatment. We have, so far, had six cases of primary lympho-sarcoma of the tonsil or in the nasopharynx, with involvement of glands, that have remained well for two years or longer after radium treatment.

II. *For local trouble in the cervical glands draining the tonsils:*

1. Simple hyperplasia of the glands at the angle of the jaw. This condition is very common in children and young adults,

and is an evidence of a chronic tonsil or nasopharyngeal infection.

2. Tuberculous cervical adenitis. We believe these cases are best treated by: (1) putting the nose and throat (the portals of entry for the tubercle bacilli) in normal condition; (2) removal or local incision and curettage of the caseating glands; (3) the judicious administration of tuberculin; and (4) general hygienic measures—with especial emphasis on the necessity of rest.

III. *For general systemic disorders secondary to a focus of infection in the tonsils:*

1. Infectious arthritis in which the periarticular changes predominate.

2. Myalgia or myositis.

3. The early stages of a glomerulo-nephritis.

4. The various nervous symptoms designated as "neurasthenia."

5. Occasionally, an iritis, refractive to all treatment, may be benefited by a tonsillectomy; but in these cases lues or tuberculosis should first be considered as an etiological factor.

6. The rare conditions, one example of which is given below, in which the chief symptoms are septic temperature; leucocytosis; general muscular and joint pains; general intoxication with negative findings on physical examination except for large, succulent tonsils.

LUDWIG BEEM.—Age 20. Med. No. 92223, Dr. L. F. Barker's service.

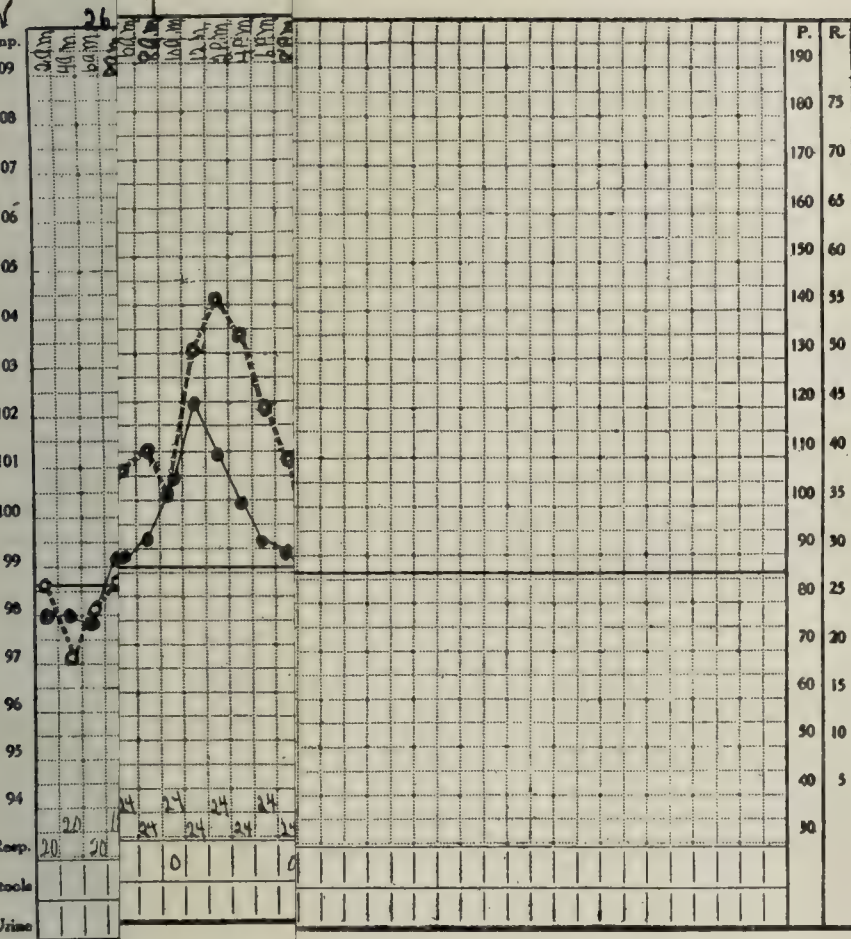
The patient was a sailor on a North German Lloyd boat that had been on the oriental service. He was admitted to The Johns Hopkins Hospital in November, 1913, complaining of chills and fever, and pains in all the joints and muscles. He had been confined to bed for a week before landing and could not walk nor move his arms or legs without great pain. There was no history of tonsillitis. The first symptom was a chill with a temperature of 105° F. The joints were slightly swollen but not red or hot. Leucocytes, 13,000.

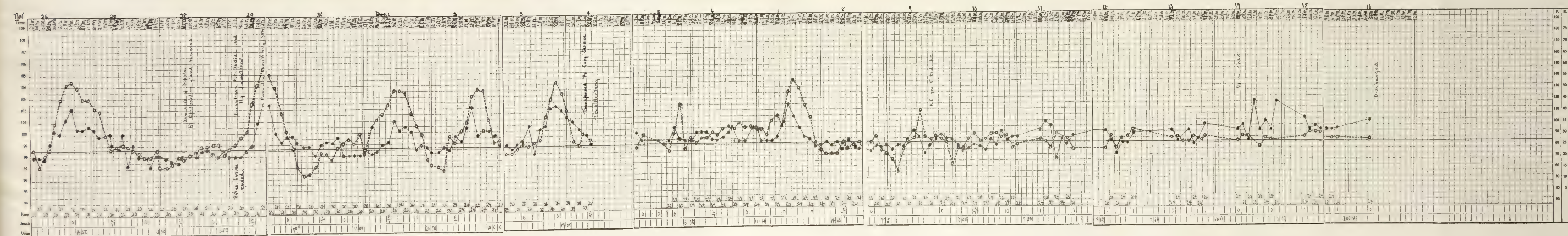
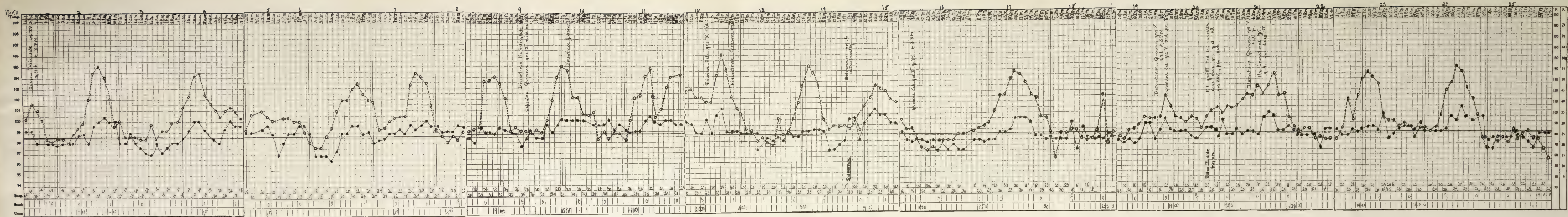
The patient was under observation in the medical ward for six weeks. During this period, the temperature curve suggested malaria, except that the elevations occurred at very irregular intervals. No malarial organisms were found on repeated examinations, and a splenic puncture was negative. Blood cultures were always negative. The Wassermann of the blood and cerebrospinal fluid was negative. The administration of Salvarsan and a course of quinine had no appreciable effect on the temperature.

The tonsils were much enlarged, but with no evidence of an acute inflammation. There was a slight general glandular enlargement.

The tonsils and adenoids were removed, after which there was a cessation of the chills (*cf.* temperature chart), and a rapid disappearance of the pain in the joints and muscles. The patient was discharged about three weeks later, and returned to his boat. Nothing has been heard from him since leaving the hospital. Cultures from the tonsils⁴⁰ showed a pure culture of a hemolytic streptococcus.

⁴⁰ Cultures from tonsils after excision are taken in the following way: The tonsil is removed with the capsule intact. A portion of the capsular surface is burned with a hot knife. A puncture is made through the burned area and culture taken by inserting the platinum loop through this opening into the parenchyma of the tonsil.





We have had two other cases in which the clinical symptoms, temperature curve, the negative findings on physical examination and the ultimate result of the tonsillectomy were identical with the above case.

IV. As a prophylactic measure:

1. In chorea, acute rheumatic fever and heart lesions, it is often advisable to remove the tonsils and adenoids in order to prevent further cardiac lesions that may result from an acute tonsillitis. The operation should never be undertaken, however, during the acute stage of the disease. There is nothing to be gained by such a procedure, and the consequences might be serious.

2. In the cases of chronic nephritis and arterio-sclerosis that give a history of repeated attacks of tonsillitis, a tonsillectomy, by preventing further acute attacks, may be of decided benefit to the patient.

The Contra-indications for Tonsillectomy:

1. A tonsillectomy should never be undertaken during the acute stage. It is best to wait at least three weeks after all symptoms have subsided. Several cases have been reported in which a cerebral (usually temporal lobe) abscess resulted from a tonsillectomy while the tonsils were inflamed. The symptoms (headache, choked disc, vomiting, etc.) first appear about three weeks after the operation.

2. Diabetes is a contra-indication for tonsillectomy as it is for any operation necessitating general anaesthesia.

3. A tonsillectomy is rarely of any benefit in the chronic deforming types of arthritis. The operation is quite severe, and in the majority of these cases, probably does more harm than good.

4. There is nothing to be gained from a tonsillectomy during the acute stage of chorea, acute rheumatic fever or endocarditis. Our experience has shown that even after the nose and throat have been put in normal condition by operative measures, chorea, rheumatic fever and endocarditis may recur. This would indicate that the tonsils are not the only portal of entry for the organisms causing these diseases.

5. As a general rule, the tonsils should not be removed in children up to fifteen years of age solely because they are enlarged or detritus is seen in the crypts. In all of these cases the adenoids are also enlarged and should be removed on account of the damage that may result from mouth-breathing and obstruction of the Eustachian tubes. It must be remembered that there is normally a hyperplasia of the tonsils and adenoids during childhood; also that the probable function of this lymphoid tissue is to protect the lower air passages, as has been fully discussed previously. Even frequent attacks of tonsillitis do not necessarily mean that the child's tonsils should be removed; often removal of adenoids, regulation of the digestive system, and general hygienic measures will prove sufficient.

6. A general anaesthetic should not be given in cases with an incipient or advanced pulmonary tuberculosis. If an operation is absolutely necessary, nitrous oxide is the anaesthetic of choice.

In cases with "latent" or "apparently arrested" tuberculous lesions, however, it is often advisable to operate on the nose and throat if the patient is subject to frequent coryza or angina attacks. The detrimental effects in these cases of acute infections of the respiratory tract (fully discussed in the preceding pages) seem to justify any operative procedure that will lessen the frequency of these acute attacks.

E. THE OPERATION AND THE POST-OPERATIVE COMPLICATIONS OF TONSILLECTOMY.

THE OPERATION.

A description of the technical procedure is unnecessary since all the essential steps are shown in the accompanying illustrations.

Ether is used in every case unless there is some definite contra-indication for the use of a general anaesthetic.

Every effort is made to keep the operative field dry. Control of hemorrhage in mouth and throat operations is of great importance. During one year eight cases of lung abscess following tonsillectomy were seen in one of the New York hospitals—all due to aspiration of blood-clots or pieces of tissue.⁴¹

The tonsils are removed by sharp incision. No snare or tonsillotome is used at any stage of the operation. All bleeding vessels are picked up with clamps, and at the end of the operation these bleeding points are ligated with fine black silk.

POST-OPERATIVE COMPLICATIONS OF TONSILLECTOMY.

The following tabulation includes all the post-operative complications in the 1000 tonsillectomies on which this report is based:

	Cases.
1. Fatalities	0
2. Bleeding after patient was sent to ward.....	38
(a) Severe ⁴² —requiring application of another ligature	12
(b) Slight	26
3. Post-operative bleeding from nasopharynx alone.....	8
4. Post-operative pneumonia	2
(Both of these patients were children; both recovered.)	
5. Acute otitis media	4
(Three of these patients were children.)	
6. Mastoiditis	0
7. Acute laryngitis	1
8. Acute bronchitis	2
9. Lung abscess	0
10. General septicæmia	0
(a) Endocarditis	0
(b) Metastatic abscess	0

⁴¹ Manges, M.: Occurrence of Abscess of the lung after tonsillectomy; with a report of nine cases in adults; *Amer. Jour. Surg.*, 1916; also Wessler, H.: Lung Suppuration after tonsillectomy; *Interstate Med. Jour.*, 1916, XXIII, 5-9. (Supplement on Roentgenology.)

⁴² The post-operative bleeding in these cases was almost invariably due to the slipping of a cat-gut ligature. This is liable to occur if there is much post-operative vomiting. For this reason we have discontinued the use of cat-gut for suture material, and for the past year have used fine black silk in all tonsil cases.

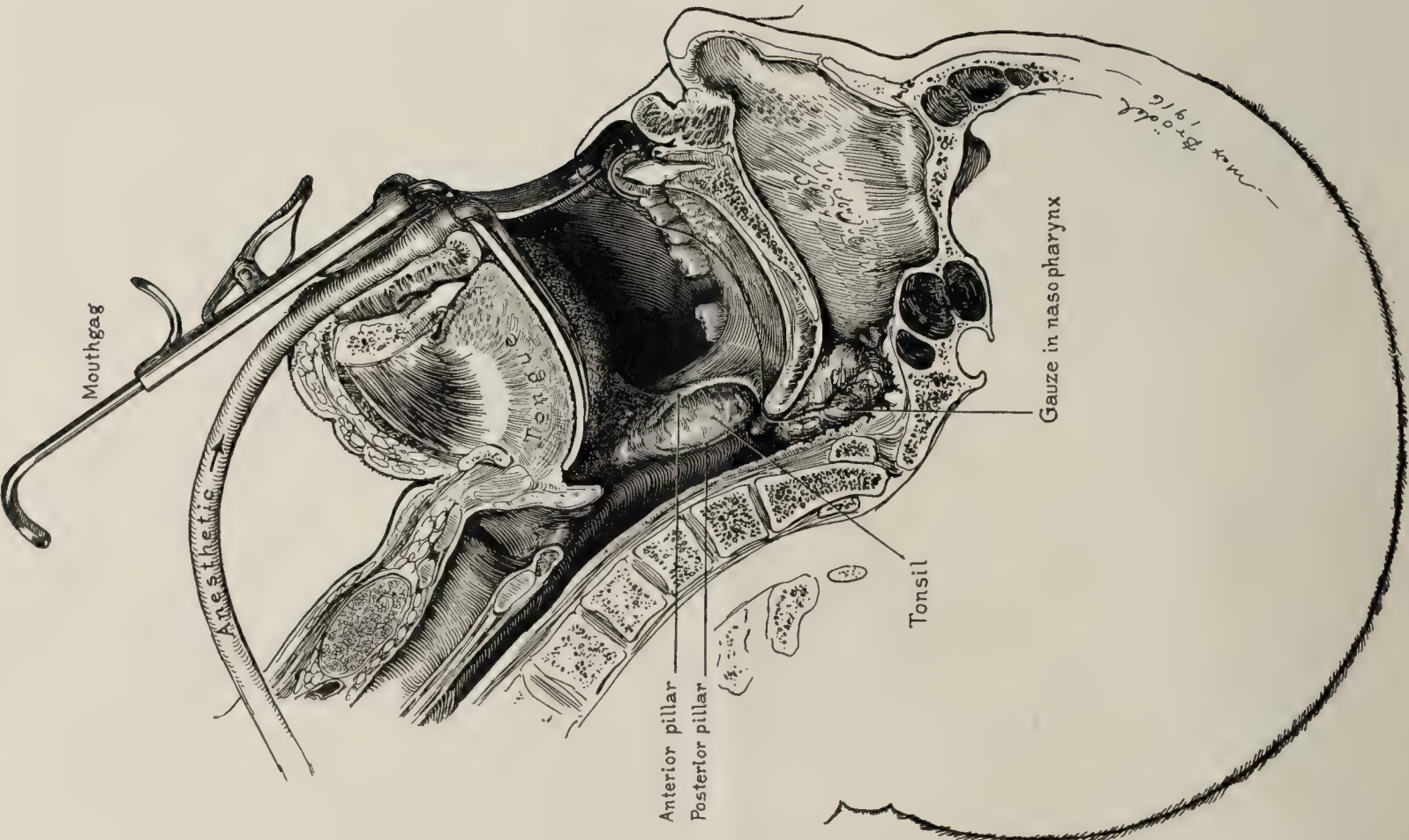


FIG. 9.—The patient is in the recumbent position. The foot of the table is slightly elevated. The gauze in the nasopharynx prevents saliva, vomitus or blood from entering the posterior nares or the Eustachian tubes. The operator stands at the end of the table. An electric head-light is worn by the operator. By placing the tongue depressor a little to the right or left of the median line of the tongue an excellent view of the operative field on that side is obtained.

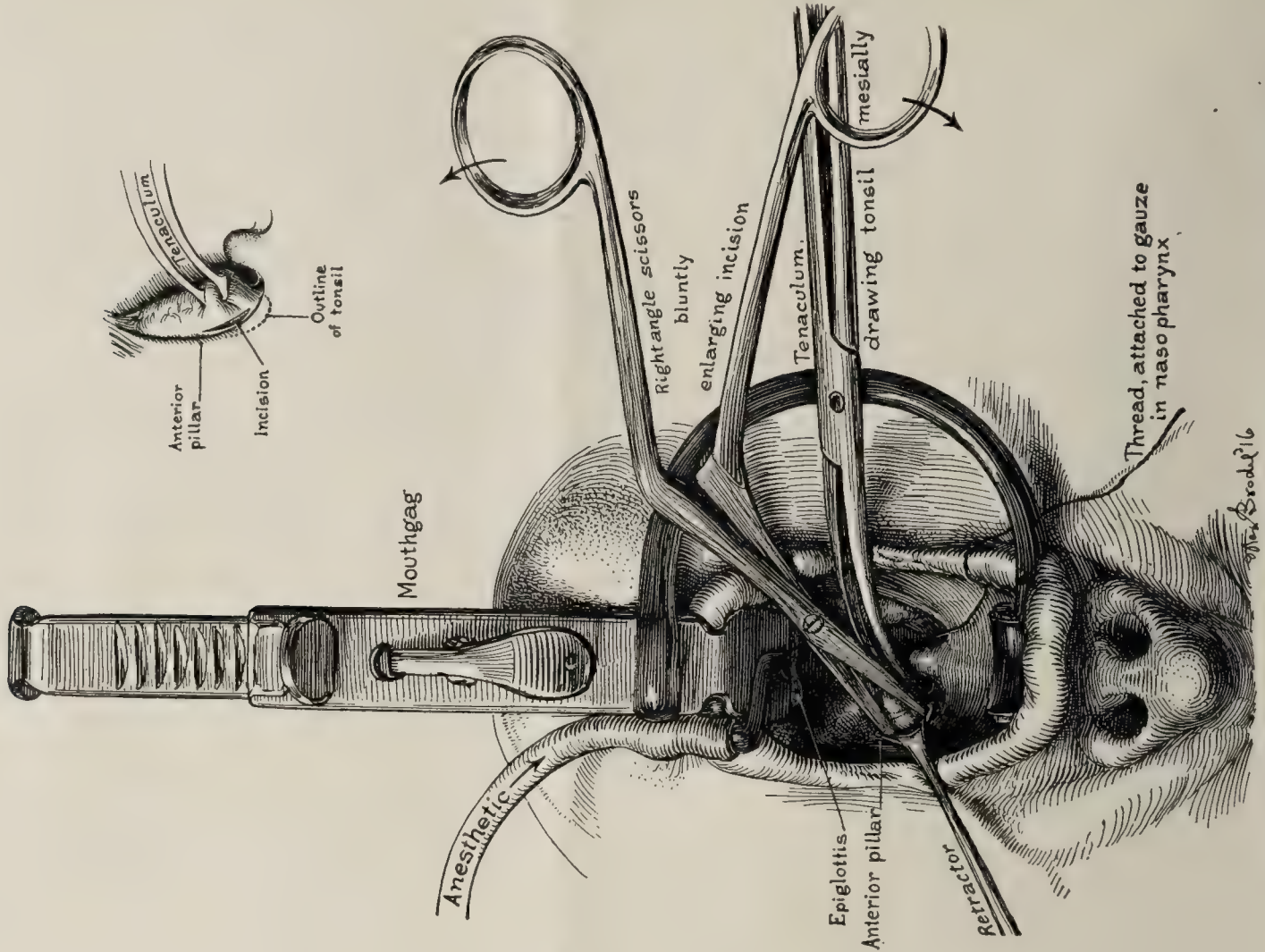


FIG. 10.—The upper pole of the tonsil is gently pulled toward the median line. An incision is then made through the mucous membrane just mesial to the anterior pillar (shown in insert). The incision is enlarged and retractor inserted as shown in large drawing.

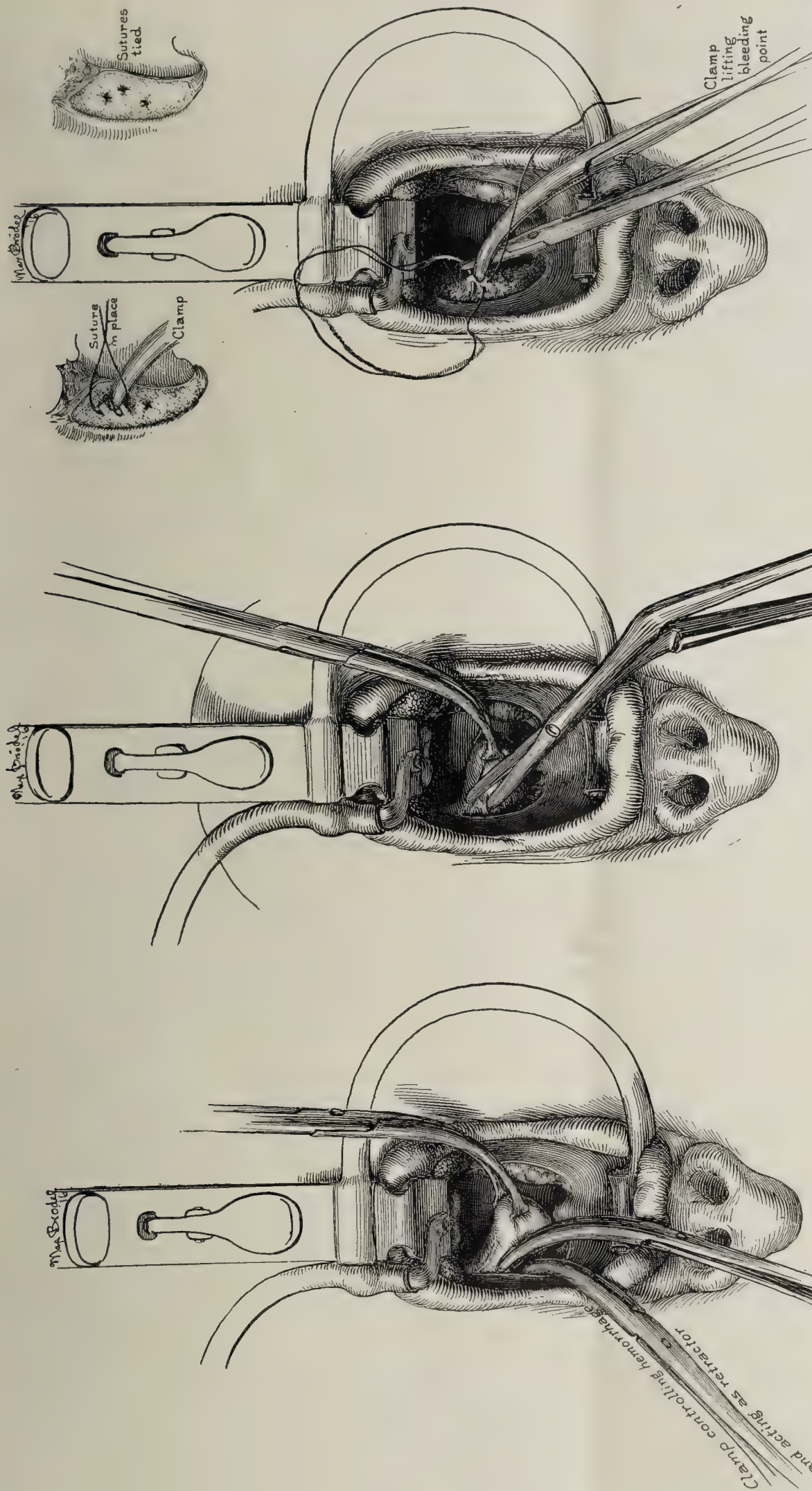


FIG. 13.—Shows the method of ligating the bleeding vessels. Note the small amount of tissue included in the clamp. The tissues are transfixed as superficially as possible, and the suture loosely tied. We have found that fine black silk is the best suture material. It is not necessary to remove the silk on a granulating surface. We have never seen a stitch abscess. Catgut may loosen if there is post-operative vomiting.

FIG. 11.—The tonsil is removed by sharp dissection. Scissors are more convenient than any form of knife. The dissection is made as close as possible to the capsule of the tonsil. The retractor is still in use at this stage of the operation, but for clearness is omitted in this drawing.

FIG. 12.—Every bleeding vessel is clamped as in any other surgical operation. This insures a dry operative field and lessens the danger of post-operative pulmonary complications.

11. Cellulitis of neck	0
(a) Suppurative cervical adenitis.....	2
12. Post-operative elevation of temperature ⁴³ without physical signs; negative blood culture; gradually subsided in ten days	3
13. Tetany	1
14. Erysipelas	1
15. Infection accessory nasal sinuses:	
Antrum	1
Other sinuses	0

We ascribe the low percentage of ear and accessory nasal sinus infections to the protection afforded by the gauze pad that is always placed in the nasopharynx before the operation on the tonsil is begun (*cf.* Fig. 9). Also to the fact that after removal of the adenoids a gauze pad is held firmly in the nasopharynx for five minutes. This usually avoids the formation of a large blood-clot.

Koplik,⁴⁴ in 1912, described three forms of infections that he has observed after tonsil operations:

1. Elevation of temperature that begins on the second or third day after operation. Nothing is found in the ears, throat, cervical glands or lungs on physical examination. The temperature gradually subsides after two weeks or more without evident endocardial lesion.

2. Reports a case with an old endocardial lesion and mild chorea that was operated on while the chorea was still active. Three days later the child had a chill followed by an exacerbation of the chorea and endocarditis. Died two weeks later.

3. Severe hematogenous infection with destructive blood changes, ecchymotic areas under the skin and throughout the intestinal tract.

Wessler⁴⁵ in 1916 reports eight cases from the medical clinic of the Mt. Sinai Hospital with a lung abscess following tonsillectomy. All of these patients were operated on at one of the nose and throat hospitals in New York and were subsequently admitted to the Mt. Sinai Hospital on account of the pulmonary symptoms.

1. Most of the patients were adults:

1 was 10 years of age.

1 was 18 years of age.

6 were from 22 to 40 years of age.

2. The onset of the pulmonary symptoms varied from one to ten days.

3. The onset of the signs of pulmonary suppuration in the majority of the cases varied from one to two weeks after operation.

4. There was a leucocytosis of from 12,000 to 26,000 in seven of the cases.

⁴³ Refer to article by H. Koplik: Infections Following Tonsillectomy, with a Consideration of the Forms of Such Infections; *Am. J. Med. Sciences*, 1912, CXLIV, 30-36.

⁴⁴ Koplik: *Loc. cit.*

⁴⁵ Wessler H.: *Loc. cit.*

5. Symptoms:

(a) Evidence of bronchopneumonia.

(b) Evidence of suppuration with chills, fever, purulent or gangrenous sputum.

(c) Hemoptysis is a constant symptom.

(d) Pain is frequently complained of, and is due to the associated pleurisy.

(e) Patients are not acutely ill; they may have chills followed by a remission of the temperature, during which period they appear entirely well, with the exception of a cough and a foul smelling sputum.

6. Physical signs:

(a) The lesion is usually deep-seated and aside from pleurisy there may be no signs.

(b) The X-ray plate shows an area of infiltration—sometimes lobar. Very rarely can a cavity be seen.

7. Localization of lung abscess:

(a) Abscess right upper lobe, 4 cases.

(b) Abscess right lower lobe, 1 case.

(c) Abscess right middle lobe, 1 case.

(d) Abscess left lower lobe, 2 cases.

8. Ultimate result:

(a) Of the eight cases six recovered without operative measures in from six weeks to five months.

(b) One recovered after removal of the affected lobe of lung.

(c) One patient is not improved.

I. Arthritis Group.

Our object in following these cases of arthritis was to determine, if possible, the types of joint lesions in which improvement may be expected after the removal of infected tonsils and adenoids.⁴⁶

We have not attempted to follow any definite classification of the joint lesions, but have divided them into four general groups.

1. *Infectious Arthritis*.—In these cases the predominating change is in the periarticular tissues, often with an effusion into the joint cavity. The onset is usually insidious, or may come on two or three weeks after an attack of acute tonsillitis. Only one joint may be involved, but in the majority of cases many of the joints are affected. There is very little, if any, elevation of temperature, and generally no redness around the affected joints. The joints are swollen and often extremely painful on motion. There is no associated endocarditis.

⁴⁶ We have had a still larger group of arthritis cases in which the focus of infection was in one of the accessory nasal sinuses. In all cases included in this report the only focus of infection found in the upper air passages was in the tonsils or adenoids. We hope to present the others in a subsequent communication.

2. *Myalgia*.—These cases are characterized by pain, stiffness and impairment of function of the muscles. There is no joint lesion.

3. *So-called "Rheumatoid Arthritis."*—The so-called "rheumatoid arthritis" is the most malign form of joint disease. Many joints are involved as a rule and often the spine. The process is progressive and tends to ankylosis of many of the joints. There is no associated endocarditis.

4. *Acute Rheumatic Fever*.—Polyarthritides; sudden onset; temperature 102° to 104° F.; often heart lesion, either endocarditis, pericarditis or myocarditis. The joints tend to clear up as the general symptoms subside, but the cardiac lesion is permanent in many cases. Our object in operating on the nose and throat in these cases is not primarily on account of the joint condition but to try and prevent a recurrence of either arthritis or endocarditis.

1. *Infectious Arthritis*.—During the past four years we have removed the tonsils and adenoids in 91 cases with an infectious type of arthritis. Of this number we have been able to follow up and note the ultimate result of the joint condition in 31. These 31 cases are given in detail in Table No. II. In 24 the joints were normal, both subjectively and objectively, at the time of the last examination. In some, the affected joints were much worse for a few days immediately following the tonsillectomy, but began to improve after two or three weeks. Often it was six or eight months before all joints symptoms entirely disappeared.

Four cases are classified as improved because the patients are now able to walk without pain. The affected joints, however, have never entirely cleared up, and since the tonsillectomy have at times been much worse.

Two are not improved, and one is in worse condition than at the time of the operation. One of these (Surg. No. 34,893) has a chronic ethmoiditis, but refuses further operative measures. It is possible that the arthritis in this case belongs in the group designated "rheumatoid arthritis."

2. *Myalgia*.—We use the term "myalgia" in speaking of these cases because there is no conclusive evidence of a myositis or an actual inflammatory process in the involved muscles. There is stiffness, tenderness, pain on motion, and sometimes a continuous throbbing pain in the affected muscles.

We have been able to obtain subsequent examinations in four cases. The indication for tonsillectomy in each of these cases was myalgia. Two patients were examined two years after the tonsillectomy, and two one year after the tonsillectomy; in all four cases the trouble had entirely disappeared. It might, of course, have cleared up, for all we know, if no operation had been performed.

These cases are given in detail in Table No. III.

3. *So-called "Rheumatoid Arthritis."*—In this group we have been able to follow up nine cases, but the lesson to be learned from these few cases is clear.

Only two of the nine cases are improved. This improvement might be due as much to the general hygienic measures they have followed as to the tonsil operation. Two are not improved, but no new joints have been become involved. Five of the nine cases are much worse. New joints have become involved, and they are, for the most part, helpless invalids.

The conclusion drawn from this group of cases is that only in very exceptional circumstances should anyone subject a patient with "rheumatoid arthritis" to an operation for the removal of the tonsils. Even in the cases that give a history of repeated attacks of tonsillitis for many years past, as in Surg. No. 35026, it is doubtful whether it is justifiable to subject them to an operation.

Patients in this group are for the most part middle-aged people. Their disease is usually well advanced when they seek medical advice. There is often a marked anæmia, and a distinct lessening of their ability to withstand pain. A tonsillectomy is one of the most trying of all surgical procedures. This is particularly true if an ether anæsthesia is used, but doubly so under local anæsthesia. On account of the danger of post-operative bleeding and the physical and mental stress of an operation under local anæsthesia we have always employed ether.

In each of these nine cases of "rheumatoid arthritis" it seemed to us and to our advisers on the Medical and Orthopedic Staffs, that the tonsil was a source of infection, and that the patient should have the benefit of the doubt. The operation was most carefully done and every effort made to prevent loss of blood, post-operative vomiting, etc. In several instances, however, it required a stay of from six weeks to three months in the hospital in order to regain the physical level on which they were at the time the tonsillectomy was performed.

These nine cases are given in detail in Table No. IV.

4. *Acute Rheumatic Fever*.—One of the characteristic features of true rheumatic fever is the frequent recurrence of the arthritic and cardiac symptoms. As a rule, the joints will clear up after each attack, but the damage to the heart is often permanent.

Removal of the tonsils and adenoids in cases of rheumatic fever eliminates one of the portals of infection and is supposed materially to lessen the frequency of the recurrences. The following chart, which is a summary of the more detailed Table No. V shows the frequency of the recurrence of acute attacks of rheumatic fever with polyarthritides in cases that have had the nose and throat put in normal condition by operative measures.

It is quite evident that the tonsils are not the only portal of entry for the organisms that cause rheumatic fever. Four of these twenty-five cases have had a recurrence after leaving the hospital; one patient was perfectly well for two years after the removal of his tonsils and then had a characteristic attack of rheumatic fever.

We have found the same tendency to recurrence in the chorea cases that have had the nose and throat put in normal condition.

SUMMARY OF 25 CASES OF RHEUMATIC FEVER WITH ESPECIAL REFERENCE TO THE RECURRENCE AFTER TONSILLECTOMY.

No. Case	Type of heart lesion.	Time observed after tonsillectomy.	Recurrence of rheumatic fever.	Condition of joints at last examination.
1	Mitral insufficiency.	3 years.	None.	Normal.
2	" "	6 months.	"	"
3	" "	1 year.	"	"
4	" "	1½ years.	"	"
5	" "	1½ years.	"	"
6	Aortic Mitral Cardiac Arrhythmia.	3½ years.	Has had 2 attacks 2 years after operation. Another 3 years after operation.	Joints normal at present time.
7	None.	3½ years.	None.	Normal.
8	Mitral insufficiency.	3 years.	"	"
9	Pericarditis.	3 years.	On 2 occasions since operation.	Joints normal at present time.
10	Mitral insufficiency.	2½ years.	None.	Normal.
11	" "	3 years.	"	"
12	Mitral insufficiency. " stenosis.	2½ years.	"	"
13	Tachycardia. Pericarditis. Aortic insufficiency. Mitral "	2 years.	"	Joints still stiff and painful.
14	None.	1½ years.	"	Normal.
15	Pericarditis.	1½ years.	"	"
16	Mitral insufficiency.	14 months.	"	"
17	None.	1 year.	"	"
18	Mitral insufficiency.	9 months.	"	"
19	" "	9 months.	"	Joints have not improved.
20	Aortic "	1½ years.	"	Normal.
21	Mitral "	2 years.	3 weeks after tonsillectomy.	Joints normal for past 1½ years.
22	Pericarditis. Myocarditis.	3½ years.	None.	Normal.
23	None.	6 months.	5 months after operation.	Joints normal.
24	Mitral insufficiency.	1 year.	None.	Normal.
25	" "	1½ years.	"	"

II. Chorea.

It is quite evident from our results that removal of the tonsils and adenoids is not a very satisfactory therapeutic or prophylactic measure in chorea. In each of these 24 cases the greatest care was taken to remedy all abnormal conditions in the nose, throat, ears and teeth. In no case was there any post-operative complication, but the ultimate result as regards the recurrence of chorea is far from satisfactory. Two cases died during the year following the tonsillectomy with acute chorea; in one, the symptoms of chorea are still present, nearly three years after the operation; in one the chorea is worse than at the time of the operation, one and one-half years ago. One case that had no symptoms of chorea before the operation has had two attacks of chorea since the tonsillectomy, one and one-third years ago.

Of the 23 cases of Sydenham's chorea in which the tonsils and adenoids were removed, eight have had a recurrence. Two of these patients have had two recurrences each, and one has had five separate attacks of chorea since the operation. We shall make every effort to follow up the 13 patients that have as yet had no recurrence of chorea in order to determine the ultimate result.

It is not an uncommon practice for internists and laryngologists to advise a tonsillectomy during the acute stage of chorea, but it is undoubtedly a dangerous procedure, and in view of our results is an entirely unjustifiable risk. A tonsillectomy when the chorea is quiescent may be advisable, but it should be done with the idea of preventing damage to the heart or joints rather than as a curative measure for the chorea.

The following chart, which is a summary of the more detailed notes in Table No. VI, is prepared in order to emphasize

SUMMARY OF 24 CASES OF CHOREA WITH PARTICULAR REFERENCE TO RECURRENCE AFTER REMOVAL OF TONSILS AND ADENOIDS.

No. Case.	Age.	Heart lesion.	Arthritis.	Time observed after tonsillectomy.	Recurrence of chorea.
1	5	Mitral insufficiency.	None.	Chorea disappeared for 14 months; then had acute chorea; multiple arthritis; dilated heart; death.	Fatal attack 14 months after tonsillectomy.
2	5	None.	Multiple arthritis.	8 months.	None.
3	4	"	None.	1½ years.	"
4	3	"	"	2 years.	"
5	9	"	"	1½ years.	Fatal attack 20 months after tonsillectomy. Chorea has never entirely disappeared.
6	7	"	"	2½ years.	None.
7	7	Mitral insufficiency.	Acute rheumatic fever, 2 attacks. (No recurrence.)	1½ years.	None.
8	8	None.	None.	2½ years.	"
9	9	Mitral insufficiency.	Acute rheumatic fever, 1 attack. (No recurrence.)	2 years.	1st recurrence 3 months after tonsillectomy. 2d recurrence 1 year later.
10	10	" "	Yes?	1½ years.	None.
11	10	" "	None.	14 months.	1st recurrence 3 months after tonsillectomy. 2d acute chorea and endocarditis 6 mos. later.
12	10	None.	"	1 year.	None.
13	9	"	"	1 year.	11 months after tonsillectomy, chorea with palsy in left arm and leg.
14	12	Mitral insufficiency. Pericarditis.	Multiple arthritis.	1½ years.	Died with recurrence of rheumatic fever.
15	11	Mitral insufficiency. " stenosis.	Multiple arthritis. (No recurrence.)	2½ years.	Symptoms of chorea have never disappeared.
16	15	Mitral insufficiency.	Acute rheumatic fever. Some joints still involved.	3 years.	None.
17	15	None.	None.	2½ years.	"
18	11	Mitral insufficiency.	"	1½ years.	"
19	14	None.	"	1½ years.	Chorea worse than at time of tonsillectomy.
20	13	"	Yes. Has cleared up.	1½ years.	None.
21	15	Mitral insufficiency.	None.	1½ years.	"
22	8	" "	Acute rheumatic fever. (No recurrence.)	3½ years.	"
23	12	None.	None.	2½ years.	Has had 5 attacks of chorea since tonsillectomy.
24	10	Mitral insufficiency. Pericarditis.	Acute rheumatic fever, 2 attacks. (No recurrence.)	1½ years.	No chorea before operation; 2 attacks since.

the frequency of cardiac and joint lesions in chorea; to show the length of time we have observed these cases after operation; and to illustrate the ultimate results as regards recurrence of choreic symptoms.

III. Nephritis.

According to Baehr,⁴⁷ Ophüls⁴⁸ and others, there is a type of renal lesion, not infrequently found at autopsy, in which the damage is primarily in the glomerular tufts of vessels. This condition is designated as a glomerulo-nephritis. It is believed to be due to a septic infection, usually with streptococci.

Baehr, who studied the kidneys in 25 cases of bacterial (streptococcus viridans) endocarditis, found on microscopical examination, glomerular lesions in 23 cases, and gave a very complete description of the process. An essential part of the pathological picture is the absence of any apparent changes in the uninvolved glomeruli. The tubules in intimate relation to the diseased glomeruli undergo a marked atrophy. They finally appear as strands of very cellular fibrous tissue surrounded with an infiltration of round cells.

The initial glomerular changes are ascribed to the occlusion of the glomerular capillaries with bacterial thrombi, and the tubular changes to an "inactivity atrophy." If the glomerular lesions are very widespread, the kidney will eventually present much the same appearance as the usual secondary contracted kidney.

Hematuria is one of the most characteristic features of the disease. Histologically, there are inflammatory changes in and about the affected glomeruli; edema of the interstitial tissues; degenerative changes in the glomerular and tubular epithelium; blood, leucocytes and casts in the tubules.

The etiology of the majority of cases is very evident in the comparatively recent history of tonsillitis, arthritis, acute rheumatic fever, or some other form of a general streptococcus infection with or without endocarditis.

Ophüls describes three stages of glomerulo-nephritis. The acute stage is characterized by symptoms of an overwhelming infection, and in the fatal cases, the renal lesion plays but a minor role in the symptom-complex. In the sub-acute cases, there is a gradual rise of blood-pressure to 180 or 200. There may be marked anæmia. Occasionally the edema is marked. In both acute and sub-acute cases, diplo-streptococci may often be found in the urine. As the disease passes into the chronic stage, the affected glomeruli become more and more fibrous, and are eventually transformed into small solid nodules of hyaline connective tissue. There is an extreme degree of endarteritis of both the small and large arteries of the kidneys. The blood-pressure is elevated. The heart is usually enlarged. The urine continues to show albumin, casts, red blood corpuscles and leucocytes. The phenolphthalein excretion is considerably diminished. Uræmia occurred in 11 of the 17 cases of Ophüls.

Baehr has been able to demonstrate streptococci in the capillaries of the affected glomeruli in five of his more acute

⁴⁷ Baehr: Glomerular Lesions of Subacute Bacterial Endocarditis; Jour. Exper. Med., 1912, XV, 330-347.
⁴⁸ Ophüls, W.: Nephritis (With a Review of Recent Literature); Jour. Am. Med. Assn., 1915, LXV, 1719-1725.

cases. The urine was not examined for organisms in any of our cases. In the chronic stage of the disease, bacteria are never found; they are apparently destroyed during the earlier stages, perhaps due to tissue and vascular changes unfavorable to their growth.

The following chart, which is a summary of the more detailed account given in Table No. VII, is prepared to show the frequency of the history of tonsillitis; the association of cardiac and joint lesions in these cases; the length of time observed after tonsillectomy; and the condition of the urine at the time of our last examination.

SUMMARY OF 18 CASES OF NEPHRITIS IN WHICH THE TONSILS WERE REMOVED AS A THERAPEUTIC MEASURE.

No. Case.	Age.	History of tonsillitis.	Heart lesion.	Arthritis.	Time observed after tonsillectomy.	Condition of urine at last examination.
1	8	Yes.	Mitral insufficiency.	Tbc. arthritis, left heel.	3 years.	Died, acute nephritis.
2	6	"	None.	None.	26 months.	Normal.
3	10	"	"	Multiple arthritis.	16 months.	"
4	12	"	"	None.	2½ years.	"
5	16	"	"	"	2½ years.	Tr. albumin; no casts or r. b. c.
6	16	"	"	"	10 months.	Normal.
7	17	None.	"	"	8 months.	"
8	12	Yes.	Mitral insufficiency. History chorea.	"	14 months.	Normal.
9	19	"	None.	"	7 months.	No recurrence chorea.
10	47	"	"	History; two attacks acute rheumatic fever; multiple arthritis.	3½ years.	Still few r. b. c. Normal.
11	25	None.	"	None.	2½ years.	Tr. albumin; no casts, w. b. c. nor r. b. c.
12	21	Yes.	"	"	8 months.	Normal.
13	36	"	Mitral insufficiency.	"	2 years.	Died pneumonia. Autopsy showed chronic diffuse nephritis.
14	30	"	None.	"	1½ years.	Normal.
15	21	"	"	"	1 year.	"
16	29	"	"	Multiple arthritis.	10 months.	"
17	26	"	History chorea. None.	Multiple arthritis.	1 year.	"
18	16	"	Mitral insufficiency.	None.	3½ years.	"

IV. Hyperplasia of the Cervical Glands.

A chronic enlargement of the deep cervical glands at the angle of the jaw, together with the past history of the patient, was the indication for tonsillectomy in 541 of the 1000 cases we are reporting. In each of these patients the enlarged glands on admission varied in size from that of a lima bean to that of a walnut. The relation of these enlarged glands at the angle of the mandible to the age of the patient is given below.

From	1 to 3 years of age	24 cases.
"	3 " 5 " " "	46 "
"	5 " 7 " " "	80 "
"	7 " 10 " " "	128 "
"	10 " 12 " " "	59 "
"	12 " 14 " " "	38 "
"	14 " 16 " " "	36 "
"	16 " 20 " " "	55 "
"	20 " 25 " " "	41 "
"	25 " 30 " " "	18 "
"	30 " 40 " " "	13 "
"	40 " 50 " " "	1 "
"	50 " 60 " " "	2 "
Total	541 "

Of these 541 cases we have been able to follow up and examine, with particular reference to the glands, 366 patients at periods varying from six months to four years after tonsillectomy.

I. Of these 366 cases, 19 now have tuberculous lesions, though they showed no clinical evidence of a tuberculous infection of the lungs or glands at the time of operation.

Six patients now have pulmonary tuberculosis.

Thirteen patients now have tuberculous cervical adenitis.

II. At the time of tonsillectomy 93 of these 541 patients had some clinical evidence of a tuberculous adenitis or of a quiescent pulmonary lesion. Of these 93 cases we have examined 54 since their discharge from the hospital.

8 of these 54 have developed pulmonary tuberculosis.

8 of these 54 have tuberculous glands of the neck.

1 died of tuberculous meningitis one year after operation.

1 has developed tuberculosis of the bones.

III. The improvement in the condition of the glands as a result of the tonsillectomy is indicated by the following:

In 122 of the 366 cases there are no palpable glands in the anterior triangles.

In 187 of the 366 cases the glands in the anterior triangles are not larger than peas.

In 36 of the 366 cases the glands are still enlarged.

In 21 of the 366 cases the glands are definitely tuberculous.

In Table No. VIII, we give in some detail the clinical history of 142 of these 366 patients. The size and situation of enlarged cervical glands at the time of the tonsillectomy is noted; the length of time the patient has been observed, and the ultimate result of the tonsillectomy as regards the enlarged glands. The 142 cases in this chart include some of the patients from each of the three groups mentioned above.

A chronic enlargement of the deep cervical glands near the angle of the jaw is such a frequent occurrence between the ages of five and 20 years that the parents, and for the most part the physicians, disregard them entirely.

Enlargement of the cervical glands due to an acute angina will usually subside within a month or six weeks, provided there is no chronic focus of infection in the area drained by these glands. Acute lymphadenitis is characterized, among other things, by tenderness of the infected glands on palpation. In the majority of children, especially among the class of patients that apply for treatment in the out-patient department, the glands at the angle of the jaw are the size of the end of the index finger or thumb; hard, not tender on palpation, and freely movable. Such a condition we have always regarded as a positive indication for removal of the tonsils and adenoids, provided there is no chronic infection of the accessory nasal sinuses, ears or scalp.

Our experience has shown that the tonsils are the most common site of the chronic infections that give rise to a hyperplasia of the deep cervical glands near the angle of the jaw.

In a large number of cases, we have had the carious teeth and alveolar abscesses alone treated, and observed the patients for a period of six months or more. The enlarged glands will rarely subside after such treatment, and we have concluded that caries and alveolar abscesses that drain into the mouth are only contributing factors. The condition of the teeth is very important, however, in the etiology of chronic infections. It was pointed out previously that removal of the tonsils without treatment of sinus infections, infected or carious teeth, may cause the patient to have attacks of pharyngitis, laryngitis or bronchitis subsequently. In this regard, the tonsils seem to protect the lower air passages.

The adenoids alone were removed in a series of cases in order to determine whether or not the glands would subside without a tonsillectomy. As a rule, they will not subside unless the infected tonsils are removed, or the general resistance becomes sufficient to overcome the infection.

As proof that the tonsils are the common source of infection, we refer to the results of the examination of the cervical glands in the 366 cases mentioned above. The object in giving the more detailed notes on 142 cases in Table No. VIII, is to convince the reader that even in the colored race, Russian Jews and peoples that live in unhygienic surroundings, it is possible for all enlarged glands in the upper portion of the anterior triangles to subside after putting the nose and throat in good condition. In 122 of our cases no palpable glands were present at the examination subsequent to the operation, and in 187 they were just palpable at the angles of the jaw.

If the statement is accepted that a chronic tonsillitis is evidenced by a hyperplasia of the adjoining cervical glands, then it is advisable always to consider the removal of the tonsils in cases with palpable glands at the angle of the jaw, particularly if the patient has some general systemic disorder.

We have attempted to point out in this paper what results may be expected from a tonsillectomy in the various types of arthritis, acute rheumatic fever, chorea and nephritis. As to whether or not a tonsillectomy is advisable in an individual case depends on the nature of the malady and the general condition of the patient.

What we wish to emphasize by presenting this group of cases is that the hyperplasia of the glands at the angle of the jaw, so common in children and young adults, is an evidence of chronic infection of the nose or throat. The most frequent situation of the chronic infection is the tonsils. Occasionally we see a patient with evident chronic tonsillitis without palpably enlarged cervical glands, but this is exceptional. When the glands at the angle of the jaw on one or both sides are palpably enlarged it is advisable to consider a removal of the patient's tonsils, regardless of their size or appearance.

In the majority of cases the enlarged glands are apparently due to a chronic pyogenic infection, and will subside after tonsillectomy; in others they are due to tubercle bacilli. In 21 of our 366 cases the glands, subsequent to the operation, gradually



FIG. 1.—M. D., age 11. Surg. No. 33468. Photograph taken in Dec., 1913. Showing large mass tuberculous glands on left side neck. Histological tubercles were found in left tonsil; no tubercles found in right tonsil. Treatment: Removal of the tonsils and local incision and curettage of the suppurating glands. General hygienic measures. No tuberculin treatment.



FIG. 2.—Photograph of patient, shown in Fig. 1, taken Oct., 1916 (nearly 3 years after tonsillectomy). There are no palpably enlarged glands on either side of the neck. The lungs are clear on physical examination. Temperature is normal. Apparently perfectly well.



FIG. 3.—J. M., age 27. Surg. No. 34742. Tonsils and adenoids removed in June, 1914. Histological tubercles were found in both tonsils. The photographs show a mass of tuberculous glands on the right side of the neck that first appeared about two years after the tonsillectomy. The lungs are not involved. Tubercle bacilli probably remained latent in these glands for two years before producing clinical symptoms.

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FIG. 4.—Showing tuberculous foci in right tonsil of W. S. W., age 7. Surg. No. 29529. The left tonsil also contains numerous tuberculous areas. No evidence of tuberculosis was found in the adenoids. This patient has been observed for over four years. The lungs are clear. The cervical glands are not palpably enlarged, and the child is apparently perfectly well.



FIG. 5.—L. B. Surg. No. 34699. Age 19. The only tuberculous focus found in this tonsil was near the capsule and is shown in the small square. The patient has been observed for more than two years. There is no evidence of involvement of the lungs or glands.

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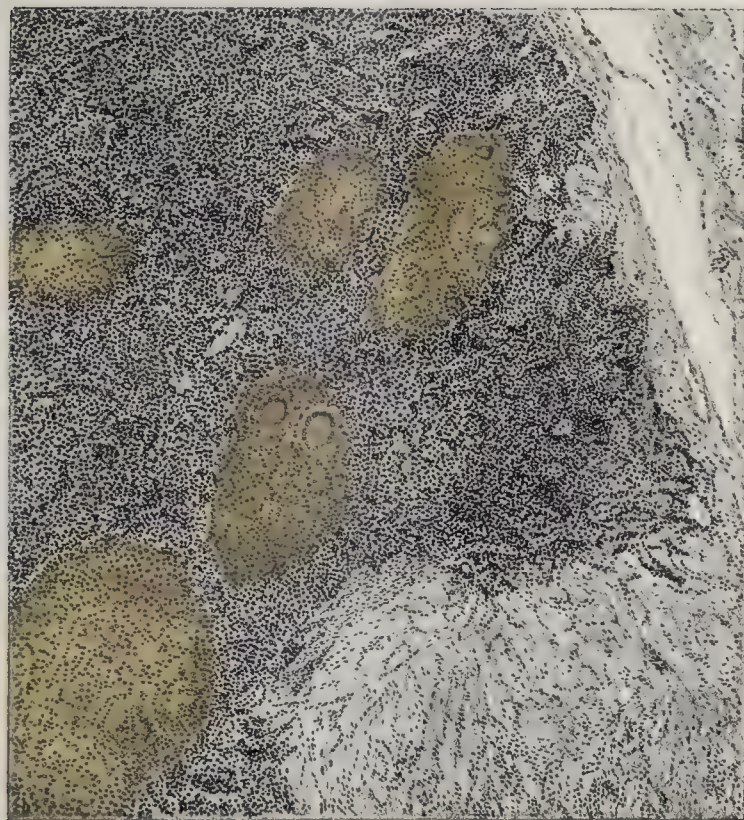


FIG. 6.—Showing the appearance of the tuberculous area indicated by the square in Fig. 5.

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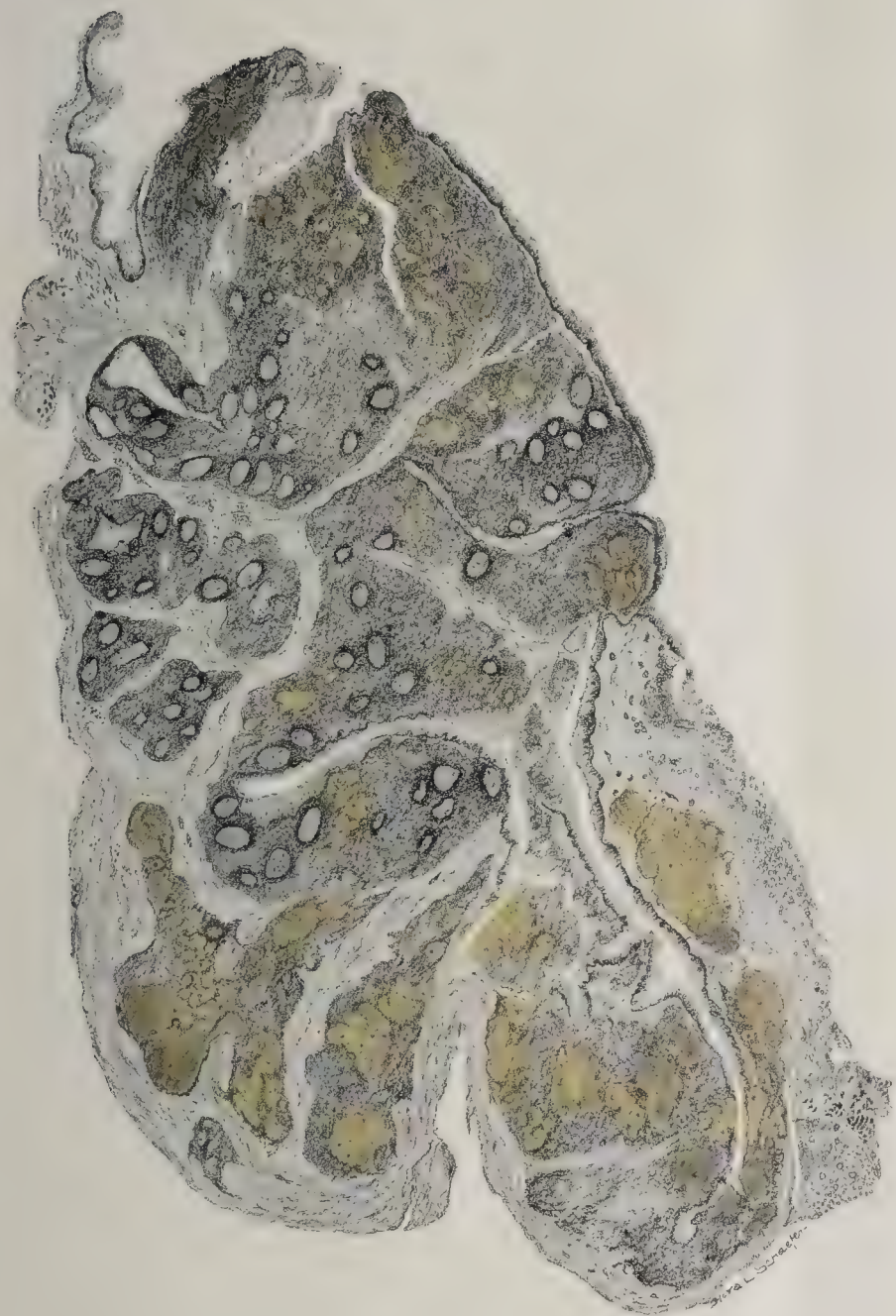


FIG. 7.—J. M. Age 27. Surg. No. 34742. The drawing shows tuberculous areas in the right tonsil. Repeated examinations during the past 2½ years have failed to show any evidence of a pulmonary lesion. Tonsils were removed in 1914. About two years later tuberculous glands began to appear on the right side of the neck. Refer to photograph of patient (Fig. 3).

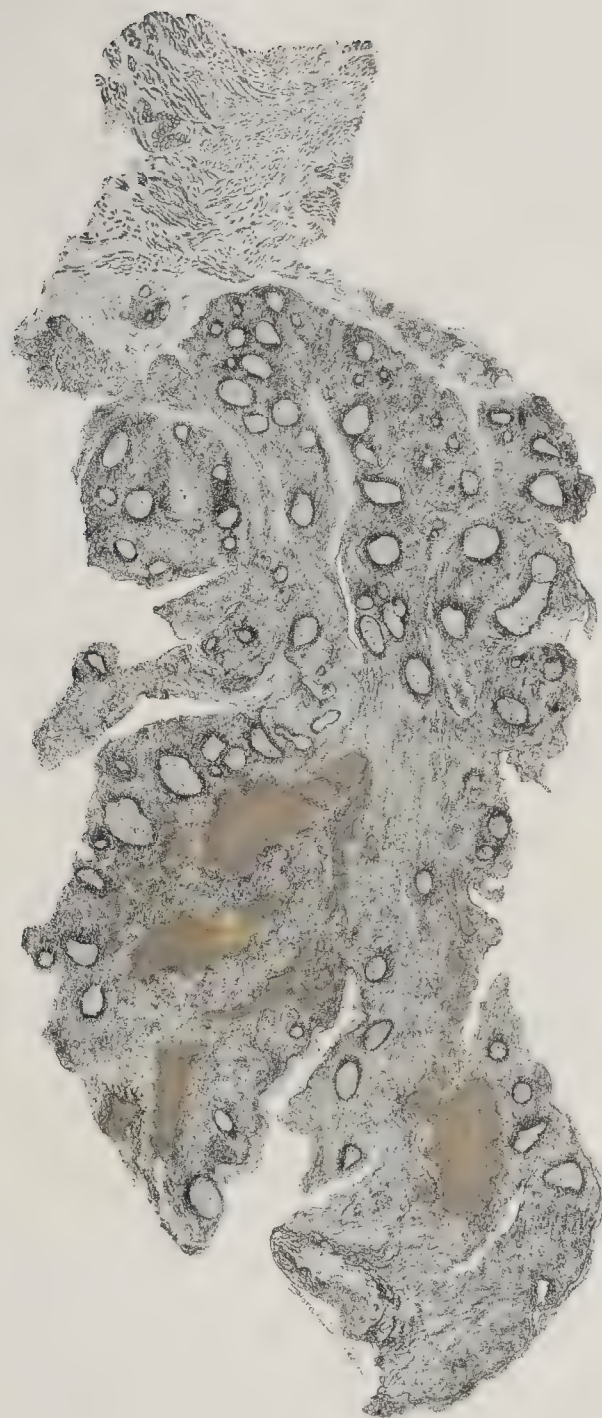


FIG. 8.—G. R. Age 7. Surg. No. 35579. Tonsils and adenoids were removed in Oct., 1914. The drawing shows tuberculous areas in the adenoids. Tonsils were not involved. The enlarged cervical glands have entirely disappeared (Oct., 1916). There has never been any evidence of a pulmonary lesion.

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assumed the characteristics of a tuberculous infection. In 36 additional cases the glands did not subside, and are treated as incipient tuberculous glands.

It is advisable that all cases with enlarged cervical glands be treated along general hygienic lines in addition to the local treatment of the nose and throat.

Tonsillectomy alone will not cure a tuberculous cervical adenitis, an arthritis or a glomerular nephritis. It is necessary in these cases to carry out all general measures that will tend to increase the patient's resistance. If the tonsils are the primary focus of infection, however, their removal may materially alter the prognosis by preventing a constant re-infection.

TABLE I.—SUMMARY OF CASES OF TUBERCULOSIS OF THE TONSILS OR ADENOIDS
I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Clinical Examination. Tonsils, Adenoids, Teeth, Nose, Ears.	Microscopical Examination.			Glands. Size, Situation, Character.	History.
				Tbc. R. Tonsil.	Tbc. L. Tonsil.	Tbc. Adenoids.		
H. W. 29528. Female. 1.	W	4	Tonsils: Much enlarged. Adenoids: Enlarged; mouth-breather. Teeth: Excellent condition. Nose: Turbinate and septum normal. Ears: Normal.	+	+	0	Enlarged in anterior and posterior triangles both sides. Size of hickory-nuts at angles of jaw; freely movable.	Brother (Surg. No. 29529) had Tbc. in both tonsils. No history of Tbc. in family. Have always had certifie milk. Nurse has no tbc. lesion. Has frequent colds.
F. C. 33258. Male. 2.	W	5	Tonsils: Almost meet in mid-line. Adenoids: Enlarged; mouth-breather. Teeth: Excellent condition. Nose: Normal. Ears: Normal.	0	+	0	Measure 5 x 8 cm. at angle of jaw on left; soft; not adherent to skin. Axillary and inguinal slightly enlarged.	No history Tbc. in family. Since attack tonsillitis 3 months ago gland neck have been enlarged; anorexia general malaise.
R. S. 33330. Male. 3.	W	4	Tonsils: Slightly enlarged. Adenoids: Enlarged; mouth-breather. Teeth: Good condition. Nose: Normal. Ears: Normal.	0	0	+	Enlarged at angle of jaw on both sides. 6 x 2 cm. on right. Soft; not adherent to skin; not tender.	Frequent sore throat. Attacks with "chills and fever." Mouth-breather difficulty in swallowing; and "knot in neck."
J. H. 34189. Male. 4.	W	5	Tonsils: Slightly enlarged; adherent. Adenoids: Small. Teeth: Normal. Nose: Normal. Ears: Normal.	+	0	0	Enlarged on both sides. 5 x 3 cm. at angle of jaw on right; hard; fixed; not adherent to skin on right. No general glandular enlargement.	No Tbc. in family. Never had sore throat. Onset with enlarged gland on right 6 months ago; on left 1 months ago. Fever for 6 months loss of appetite.
N. N. 36033. Male. 5.	C	5	Tonsils: Small, adherent. Adenoids: Large. Teeth: Carious. Nose: Normal. Ears: Drums intact; retracted; hearing impaired.	+	+	Sections lost.	Enlarged on both sides, particularly on right. Hard, movable. Diag. in Phipps Dispensary is tuberculous cervical adenitis.	Pneumonia and measles at 2; frequent colds; bad hearing; no discharge from ears.

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

E. M. 29388. Male. 6.	W	8	Tonsils: Very large. Adenoids: Large mass; mouth-breather. Teeth: Many carious. Nose: Normal. Ears: Normal.	0	0	+	Enlarged in anterior and posterior triangles on both sides; hard; discrete; no matting.	Frequent attacks tonsillitis for past 6 years. Has had nearly all children's diseases. Mouth-breather all his life. No family history of Tbc.
R. B. 30491. Male. 7.	W	10	Tonsils: Slightly enlarged; not adherent. Adenoids: Small mass. Teeth: Few carious.	+	0	Sections lost.	Glands neck not palpable on either side.	No history suggesting Tbc. in patient or family. Never had sore throat. Is mouth-breather.
R. H. 31504. Male. 8.	C	9	Tonsils: Much enlarged. Adenoids: Large mass. Nose: Normal. Teeth: Good condition.	+	Sections lost.	Sections lost.	Enlarged on both sides; hard; matted; not adherent to skin. Very suggestive of tbc. glands.	No history of Tbc. No previous illness. Was backward in walking and talking. Mouth-breather.
C. M. 32187. Male. 9.	W	9	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Carious. Ears: Normal.	0	0	+	At angle of jaw measure 2 x 3 cm. Hard; freely movable; not adherent.	No history of Tbc. in family. Only previous illness measles. Frequent attacks tonsillitis with marked swelling glands neck.
H. P. 33070. Male. 10.	W	10	Tonsils: Enlarged; right larger than left. Adenoids: Small amount. Teeth: Very bad condition. Nose: Deflected septum. Ears: Normal.	+	0	Sections lost.	Enlarged on both sides in anterior and posterior triangles. 2 x 3 cm. at angle of jaw on both sides. Hard; movable; not tender; not matted.	Congenital lues? No history of Tbc. in family. Frequent attacks tonsillitis.
A. C. 33385. Male. 11.	C	10	Tonsils: Much enlarged. Adenoids: large mass. Teeth: Good condition. Ears: Normal.	0	0	+	Enlarged in anterior and posterior triangle both sides. Hard; movable; not matted.	No history of Tbc. in family. Has had measles, diphtheria, pneumonia and poliomyelitis. Almost constant sore throat for past 3 years. Frequent febrile attacks.
G. R. 35579. Female. 12.	W	7	Tonsils: Much enlarged. Adenoids: Large. Teeth: Good condition. Ears: Normal.	0	0	+	Enlarged both sides neck, hard; not matted; not tender.	Frequent attacks tonsillitis for past 2 years. Glands neck much enlarged with each attack.
E. K. 36818. Male. 13.	W	7	Tonsils: Enlarged; adherent. Adenoids: Large. Teeth: Carious. Ears: Normal.	0	0	+	Enlarged at angles of jaw on both sides. Hard; movable; not tender; not matted.	Frequent attacks tonsillitis. Frequent attacks arthritis. Frequent attacks fever. No history Tbc. in family.
C. N. 37805. Female. 14.	W	7	Tonsils: Enlarged; adherent. Adenoids: Enlarged. Teeth: Carious. Ears: Normal. Nose: Normal.	+	+	+	At angle jaw on right 4 x 3 cm. Enlarged on left and in posterior triangles.	Has had scarlet fever and diphtheria. No history sore throat. Mouth-breather. No history of Tbc. in family.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

General Physical Examination. Tuberculin Test.	Temp. (Mouth) on Day Before Operation. ° F.	Date and Indication for Operation.	Post-operative Complications.	Subsequent Examination.
No general glandular enlargement. Lungs and heart: Normal. Urine: Trace of albumin. Spleen: Not palpable.	98.6	Mar., 1912. Enlarged cervical glands and mouth-breathing.	None.	April, 1915 (3 years after operation). No palpable glands. Colds infrequent; breathing normal. General health excellent. Oct., 1916. Perfectly well. No symptoms of Tbc. of cervical glands or lungs.
Heart and lungs negative. W. B. C.: 7800. Hb.: 71%.	99	Nov., 1913. Enlarged cervical glands and mouth-breathing.	None.	On the day following the operation the glands had decreased to one-half former size. Jan., 1914 (3 months after operation). Glands still palpable but not visible. Has gained weight. General condition improved. Oct., 1916. General health good. Cervical glands: Not palpable in anterior triangles; just felt in posterior triangles. Lungs: Normal on physical examination.
Heart and lungs normal. No general glandular enlargement. Pirquet positive.	99	Nov., 1913. Enlarged cervical glands; mouth-breather; frequent sore throat.	None.	June, 1915 (19 months after operation). Glands barely palpable on both sides. Temperature normal. X-ray of chest reported normal. Pirquet test positive. Oct., 1916. General health good. Weight 50 pounds. Glands at angles jaw not palpable. Just felt in both posterior triangles. Jan., 1915. Has been kept quiet; temperature to 99.2° F. evening; appetite good. Examination at H. L. H. Lungs negative. Glands on right fluctuate—opened, local curettage.
Heart, lungs, kidneys normal. X-ray chest normal. Tbc. skin test positive.	99-105	Mar., 1914. Tbc. glands neck right.	None.	Mar., 1915. Otitis media acute on right; other glands suppurate on right; opened. Nov., 1915. Fistula healed. Lungs normal. Glands on left not palpable; on right measure 3 x 2 cm. No other glands enlarged. Weight 67 pounds. Temperature normal for past 3 months. Is still kept quiet. Jan., 1916. Temperature normal for over a year. Glands on right barely palpable. General health excellent.
Retrosternal dullness. Dullness at both apices. No râles heard. Spleen palp. Tbc. skin test positive.		Jan., 1914. Enlarged glands. Mouth-breathing.	None.	Sept., 1915 (21 months after operation). Has gained weight; no colds since operation; cervical glands size lima beans; discrete; hard; movable. X-ray of chest: Marked enlargement mediastinal glands. Wassermann negative. Oct., 1916. General health good. Glands about same as in above note. Teeth carious. Nose and throat look normal. Temperature 98.6° F. Weight 42 pounds. Slight impairment of percussion note at both apices; no râles. Skin test O. T. positive. X-ray report: Enlarged mediastinal glands; chronic infiltration of both lungs, probably tuberculous. Sent to dental department.

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

Undersized. Physically and mentally 4 years retarded. Lungs: Percussion note impaired to 3d rib on both sides. No general glandular enlargement. W. B. C.: 14,000. Hb.: 75%. Tbc. skin test positive.	99	Mar., 1912. Enlarged cervical glands; mouth-breather; frequent tonsillitis; retarded development mentally and physically.	None.	June, 1915 (over 2 years after operation). Glands barely palpable. Has grown and gained in weight. Marked improvement in mentality. No colds or sore throats since operation. Lungs: Still impairment of percussion note over both uppers; no cough; appetite good; tuberculin tests still positive; skin and 1% Calmette (eye). Oct., 1916. General health excellent. Has grown rapidly. Glands: Not palpable at angle jaw right; just felt on left and in posterior triangles. Lungs clear on physical examination (Phipps Dispensary). Skin test O. T. positive.
No glandular enlargement. Lungs: Normal. Heart: Evidence of old endocarditis. Spleen: Not enlarged. Some general glandular enlargement. Rickets; rosary; enlarged ends long bones. Lungs and heart normal. Tbc. skin test positive.	99	Sept., 1912. Mouth-breathing and heart condition. Feb., 1913. Enlarged glands of neck.	None.	Jan., 1916 (over 3 years after operation). In perfect health. Glands not palpable. Lungs normal.
Some general glandular enlargement. Heart and lungs normal. Von Pirquet positive.	98.6	May, 1913. Frequent attacks tonsillitis; mouth-breather; acute attack cervical adenitis.	None.	Jan., 1915 (2 years after operation). Glands anterior and posterior triangles not palpable. Lungs normal. General health excellent. Tbc. skin test positive. Oct., 1916. General health good. Cervical glands not palpable on either side. No sore throat since operation. No cough. Nose, throat and ears look normal. Weight 77½ pounds. Lungs, heart, abdomen normal on physical examination (Phipps Dispensary). Tuberculin skin test O. T. negative. Wassermann positive. Urine normal.
General glandular enlargement (lues). Heart and lungs normal. W. B. C.: 9000. Hb.: 78%.	99.8	Oct., 1913. Frequent attacks tonsillitis (carious teeth pulled at same time).	None.	June, 1915 (1½ years after operation). Gland at angle jaw on left 1.5 x 3 cm.; barely palpable on right. Carious lower molar teeth may account for enlarged glands. Has skin lesions suggestive of tuberculids. Since operation on tonsils one of glands on left side of neck has suppurated; was treated by local incision and curettage; is not healed. No general glandular enlargement. Spleen not felt. Lungs clear. Pirquet test positive.
General glandular enlargement. Ascaris infection. Heart and lungs normal.	98.6	Dec., 1913. Frequent attacks tonsillitis. Swelling cervical glands. Headaches.	None.	July, 1915 (1½ years after operation). Glands in anterior triangle not palpable; just felt in posterior triangles. Teeth very bad condition. The axillary, inguinal and epitrochlear glands enlarged. No headaches since operation. No sore throat since operation. Wassermann positive. Oct., 1916. General health good. Nose, throat and ears are normal. Cervical glands not over ½ cm. diameter. Temperature normal. Weight 82 pounds. Epitrochlears still enlarged. Wassermann still positive. Tuberculin test skin O. T. positive.
Heart and lungs normal. No general glandular enlargement. Liver 2 f. b. below c. m. Pirquet positive.	98	Oct., 1914. Frequent attacks tonsillitis. Mouth-breathing. Enlarged cervical glands.	None.	June, 1915 (8 months after operation). Gland at angle jaw on left 2 x 1 cm.; hard; movable. Just palpable on right and in posterior triangles. No general glandular enlargement. Spleen not felt. Liver same size as previous examination. Lungs normal. Pirquet positive. Oct., 1916. General health good. Gland on left much smaller; size shot in posterior triangles and on right in anterior triangle. Nose, throat and ears look normal.
Heart: Aortic and mitral insufficiency and stenosis. Lungs: Normal. No general glandular enlargement.	98.4	April, 1915. Frequent attacks tonsillitis, endocarditis, rheumatic fever. Enlarged cervical glands.	None.	Oct., 1916 (18 months after operation). General health good. No sore throat since operation. Pain in knees, ankles and arms 6 months ago; no swelling; was not in bed. Joints now normal. Glands neck not larger than 1 cm. in diameter on either side. Nose, throat and ears normal. Lungs examined in Phipps Dispensary; no tuberculous pulmonary condition. Heart as before. Skin O. T. +.
Lungs: Normal on percussion and auscultation. X-ray: Mediastinitis. Pirquet positive. No general glandular enlargement.	100	Sept., 1915. Enlarged cervical glands right. Mouth-breather. (Carious teeth pulled.)	None.	Nov., 1915 (2 months after operation). Glands same as at operation. On right is hard, not adherent. Temperature 99-100° F. Jan., 1916 (4 months after operation). Glands on right smaller; now measure 3 x 1 cm.; still hard. Temperature normal to-day. Oct., 1916. Gland on right slightly smaller; hard; movable. Glands in other triangles just palpable. General condition much improved. Nose and throat look normal. Removal tuberculous glands neck on right. To have tuberculin treatment.

TABLE I.—SUMMARY OF CASES OF TUBERCULOSIS OF THE TONSILS OR ADENOIDS
II. CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Clinical Examination. Tonsils, Adenoids, Teeth, Nose, Ears.	Microscopical Examination.			Glands. Size, Situation, Character.	History.
				Tbc. R. Tonsil.	Tbc. L. Tonsil.	Tbc. Adenoids.		
A. S. 37093. Male. 15.	C	8	Tonsils: Much enlarged. Adenoids: Enlarged. Nose: Normal. Ears: Normal. Teeth: Good.	+	0	0	Mass glands at angle jaw on both sides. Measures 6 x 4 cm. left; 2 x 3 cm. right. Numerous small glands in both posterior triangles. Not adherent to skin; not tender; hard.	Frequent tonsillitis; frequent "colds in head." Glands in neck get larger at times and then almost disappear for a while.
E. R. 38151. Female. 16.	W	10	Tonsils: Enlarged; especially left. Adenoids: Large. Teeth: Many carious. Ears: Normal. Nose: Normal.	0	+	0	Enlarged at angle of jaw and submaxillary triangles both sides. Hard; not adherent.	Several of the infectious children's diseases. Frequent tonsillitis. Mouth-breather. Frequent headaches. Grandmother died pulmonary Tbc. Mother has pulmonary Tbc.
O. F. 38597. Female. 17.	C	10	Tonsils: Much enlarged. Adenoids: Large; mouth-breather. Ears: Not infected. Teeth: Carious. Nose: Discharge; otherwise normal.	0	+	0	Slightly enlarged in all triangles; about 1 cm. in diameter at angle jaws.	Frequent tonsillitis and mouth-breathing.
A. B. H. L. H. 7626. Male. 18.	W	10	Tonsils: Enlarged; adherent. Adenoids: Large. Teeth: Good. Ears: Normal. Nose: Normal.	+	0	0	Large mass 4 x 8 cm. at angle jaw left. Adherent; matted together. Numerous discrete, hard glands in right anterior triangle and both posterior triangles.	No history Tbc. in family. Pneumonia twice. Frequent tonsillitis for past 2 years.

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	Special Examination. Tonsils, Adenoids, Teeth, Nose, Ears.	Microscopical Examination.			Glands. Size, Situation, Character.	History.
					Tbc. R. Tonsil.	Tbc. L. Tonsil.	Tbc. Adenoids.		
J. B. 31047. Female. 19.	W	14	School.	Tonsils: Much enlarged; right larger than left. Adenoids: Large mass. Teeth: Carious. Nose: Normal. Ears: Normal.	+	+	0	On left mass measures 6 x 10 cm. with chain of enlarged glands to clavicle. On palpation are fluctuant, adherent to skin, and matted together. Glands barely palpable on right or in posterior triangles.	No history of Tbc. in family. Measles, varicella, scarlet fever. Frequent attacks of tonsillitis. Almost constant left-sided sore throat. No night-sweats or cough. Onset 1 year before admission with swelling glands left-side neck.
F. N. 31486. Male. 20.	W	9	School.	Tonsils: Enlarged; left larger than right. Adenoids: Large mass. Nose: Negative aside from discharge due to adenoids. Ears: Not infected. Teeth: Carious.	0	+	0	Mass glands left at angle jaw; measure 7 x 5 cm. fluctuate; adherent to skin. Typical tbc. glands.	Frequent colds; no history tonsillitis. Gland began to enlarge on left 1 year ago. Has at times almost disappeared. Recently became rapidly enlarged; never painful.
M. D. 33468. Female. 21.	W	11	School.	Tonsils: Had been partially removed because enlarged; since then frequent sore throats. Adenoids: Had been removed. Teeth: Carious. Ears: Normal. Nose: Normal.	0	+	No tissue removed at opn.	On left mass measuring 8 x 10 cm. Adherent to skin; fixed to underlying tissues; soft. But slightly enlarged on right and in posterior triangles.	No history of Tbc. in family. Mumps, whooping cough and measles. Following tonsillitis 5 month ago glands neck on left began to swell. Never tender. No coughs; night-sweats or loss of weight. Appetite poor.
M. H. 35638. Female. 22.	C	14	School.	Tonsils: Much enlarged. Adenoids: Small amount. Teeth: Good. Ears: Normal. Nose: Hypert. inf. turb., double.	+	+	Sections lost.	On left mass of glands at angle of jaw measuring 5 x 7 cm.; firm; not tender; movable; not adherent to skin. Small discrete glands along sternomastoid on right and in posterior triangles.	No history of Tbc. in family. Frequent sore throats for past 4 years. Some loss of weight; loss of appetite; night-sweats. First noticed enlarged glands neck 2 weeks ago; after cold.
M. F. 35652. Female. 23.	W	13	School.	Tonsils: Much enlarged; not adherent to pillars. Adenoids: Large. Nose: Deflected septum. Ears: Chronic catarrhal otitis media. Teeth: Good.	+	0	0	Mass glands at angle jaw right and under sternomastoid 6 x 4 cm.; fluctuates; matted together. Numerous discrete glands on left and in both posterior triangles.	No history of Tbc. in family. History of sore throats and headache. Enlarged gland first noticed June, 1914, following abscessed tooth.
I. G. 36761. Male. 24.	W	12	School.	Tonsils: Not enlarged; adherent. Adenoids: Large mass. Nose: Purulent discharge right one due to infection frontal and antrum. Hypert. inf. turb. right. Ears: Normal. Teeth: Carious.	0	0	+	Mass of glands at the angle of the jaw on both sides measuring 5 x 3 cm. Enlarged glands in posterior triangles on both sides. All glands are hard; some peradenitis; not adherent to skin.	Frequent attacks tonsillitis. Mouth-breather. Frontal headaches. Dyspnoea on exertion. Enlarged cervical glands noted for one year.
M. W. 37485. Female. 25.	W	15	School.	Tonsils: Were partially removed 10 years ago. Adenoids: Large mass; mouth-breather. Ears: Chronic catarrhal otitis media. Nose: Hypert. inf. turb.; sinuses clear. Teeth: Good.	0	0	+	Enlarged glands on both sides neck at angle jaw; matted together. On right they are adherent to skin and fluctuate.	Frequent sore throat; nausea; "often has fever"; glands neck swell and subside at frequent intervals for 2 years. Had asthma when a child; none for several years past.
E. B. 37521. Male. 26.	C	12		Tonsils: Were partially removed 3 years ago. Adenoids: Large mass; mouth-breather. Ears: Chronic catarrhal otitis media; deafness. Nose: No sinus infection; otherwise normal. Teeth: Good.	0	0	+	Slightly enlarged on both sides in anterior and posterior triangles. Not tender; discrete; movable.	Came to dispensary on account impaired hearing. Has frequent sore throat and almost continual "cold in head." Never any discharge from ears.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

General Physical Examination. Tuberculin Test.	Temp. (Mouth) on Day Before Operation. ° F.	Date and Indication for Operation.	Post-operative Complications.	Subsequent Examination.
ngs: Clear on posterior and anterior. art: Normal. ine: Normal. B. C.: 12,700. .: 75%. leen: Not palpable. neral glandular enlargement. neral glandular enlargement. Lungs and heart normal. Pirquet positive. ray: Marked mediastinitis.	98	May, 1915. Chronic tonsillitis. Cervical adenitis.	None.	Dec., 1915. Died of tuberculous meningitis.
art: Normal. ngs: Clear on perc. and ausc. leen: Not palpable. neral glandular enlargement. ine: Normal. o general glandular enlargement. Spleen not felt. Heart and lungs normal on perc. and ausc. ray: Lungs practically normal. rquet positive.	99	Oct., 1915. Frequent tonsillitis. Mouth- breather. Enlarged cervical glands.	None.	Nov., 1915 (1 month after operation). Glands at angles of jaw measure 1 x 1 cm. General condition and appetite improved. Breathing normal. Oct., 1916. Temperature 99° F. Weight 76½ pounds. Nose and throat normal. Lungs clear on physical examination (Phipps Dispensary). Skin test O. T. positive. Sent to dental department on account carious teeth. Glands at angle jaw smaller. Sept., 1916. General health good. Temperature 99.4° F. Lungs clear on perc. and ausc. Skin test +. Weight 75 pounds. Cervical glands not palpable. (The slight elevation temperature probably due to coryza.)
art: Normal. ngs: Clear on perc. and ausc. leen: Not palpable. neral glandular enlargement. ine: Normal. o general glandular enlargement. Spleen not felt. Heart and lungs normal on perc. and ausc. ray: Lungs practically normal. rquet positive.	98.6	Dec., 1915. Chronic tonsillitis. En- larged adenoids. (Extraction carious teeth.)	None.	June, 1915 (1 month after operation). Glands same. Temperature 99° F. evening. Aug., 1916. No glands palpable on either side neck. Temperature never above normal for past 8 months. General health excellent.
art: Normal. ngs: Clear on perc. and ausc. leen: Not palpable. neral glandular enlargement. ine: Normal. o general glandular enlargement. Spleen not felt. Heart and lungs normal on perc. and ausc. ray: Lungs practically normal. rquet positive.	100	May, 1915. Frequent tonsillitis. Clini- cally tbc. glands neck.	None.	

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

General Physical Examination. Tuberculin Test.	Temp. (Mouth) on Day Before Operation. ° F.	Date and Indication for Operation.	Post-operative Complications.	Subsequent Examination.
o general glandular enlargement. En- larged cervical glands left. Heart and lungs normal. Liver and spleen not palpable. dneys: Albumin .5 gm. to liter; few casts; few red blood cells. lood: W. B. C. 8000; Hb. 87%.	99	Dec., 1912. Tuberculous glands left. Frequent tonsillitis. (Incision and local curettage tbc. glands on left at same time.) Advised tuberculin treatment. Carious teeth extracted.	None.	Jan., 1916 (over 3 years after operation). Has had tuberculin treatment since operation. There is no discharging sinus in neck. Glands are not palpable in anterior triangles on either side; few discrete, hard, movable glands in posterior triangle on left. No general glandular enlargement. Teeth in good shape. Throat looks normal. Lungs clear. General health excellent. Moved to Harrisburg, Pa.
heart: Normal. ngs: Clear on perc. and ausc. B. C.: 10,000. b.: 75%. o general glandular enlargement.	99.6	Feb., 1913. Tbc. glands neck left. Mouth-breather. (Extraction carious teeth. Incision, drainage tbc. abscess neck left.)	None.	Feb., 1916 (3 years after operation). Patient refuses to return for examina- tion. Nurse reports he is healthy looking boy, and that there are no enlarged glands on inspection. Goes to school regularly.
o general glandular enlargement. En- larged cervical glands left. Heart and kidneys normal. ngs: Normal with the exception of a few râles at right base. pc. skin test positive. B. C.: 9500. b.: 73%.	98.6	Dec., 1913. Tbc. cervical glands left. Tonsillitis attacks. Tuberculin treat- ment advised. Carious teeth ex- tracted.	None.	Dec., 1915 (2 years after operation). Has had tuberculin treatment. The glands at angle of jaw on left have suppurated, been treated by local incision and curettage; at present sinus healed leaving three incon- spicuous scars. There is still visible fullness on left side neck, but about one-fourth as large as at operation in 1913. General health excellent. Lungs clear. Teeth carious. Throat looks normal. April, 1916. Glands barely palpable on left side neck; not palpable on right. General health excellent. Pirquet markedly positive. X-ray chest suggests tbc. apices on both sides; no physical signs or râles; tempera- ture normal; appetite good. Weight 98½ pounds. Oct., 1916. Health good. Weight 115 pounds. Shotty glands in posterior triangles of neck; palpable glands at angles of jaw. Throat normal. Chest (H. L. H.) normal.
eneral glandular enlargement. Tbc. cervical glands left. heart: Normal. ngs: No physical signs of Tbc. idneys: Albumin and a few casts. almette: Positive.	98-101	Nov., 1914. Frequent sore throats. Tbc. cervical glands left. (Tubercu- lin treatment advised.)	None.	June, 1915 (8 months after operation). Has had tuberculin treatment. No improvement in glands neck. The mass at angle of jaw on left is larger than in Nov., 1914; measures 7 x 8 cm.; matted together; still hard. Above clavicle in posterior triangle on left there is a mass of enlarged glands. Throat looks normal. No cough; has gained weight since operation. Lungs: No signs of pulmonary Tbc. Advised to re-enter hospital for removal of tbc. glands neck.
o general glandular enlargement. Tbc. cervical glands right. heart: Normal. ngs: Clear on perc. and ausc. idneys: Normal. bc. skin test positive.	98.8	Nov., 1914. Tbc. cervical glands right. History tonsillitis. Tuberculin treat- ment advised. (Incision and local curettage.)	None.	Aug., 1915 (10 months after operation). Has had tuberculin treatment. The incision for drainage glands on right side neck is healed. The glands on right side neck barely palpable; none larger than 1 cm. in diameter; all discrete. There are a few glands of the same size and character in anterior triangle on left. Throat looks normal. No general glandular enlargement. Lungs normal. General health excellent. Oct., 1916. Temperature 98.8° F. Weight 100 pounds. Cervical glands just palpable. Lungs clear on physical examination (Phipps Dispensary). Skin test O. T. positive (very slight). General health excellent.
heart: Mitral insufficiency; heart not enlarged. ngs: Clear on perc. and ausc. idneys: Normal. ray: Shows frontal and antrum in- fection on right.	98.7	April, 1915. Enlarged cervical glands at angle jaw on both sides. Tonsil- litis. Mouth-breather. Heart lesion. (Extraction carious teeth.) (Crush- ing back inf. turb. rt.)	None.	Dec., 1915 (9 months after operation). Glands at angle of jaw on each side measure 1 x 2 cm.; hard; movable. No palpable glands in posterior triangles. Has rapidly gained weight since operation. Appetite good. No headaches; no discharge in right side nose. Heart: Same as before. Lungs: Clear.
heart: Normal. ngs: Clear on perc. and ausc. pleen not palpable. o general glandular enlargement. rine normal. kin and eye test positive.	98.5	July, 1915. Tbc. glands neck double. Chronic tonsillitis. Mouth-breather. (Excision infected tbc. gland right.)	None.	Nov., 1915. Wound neck healed perfectly. Glands barely palpable on left and in posterior triangles. There is an indefinite, deep mass under the scar on the right. Throat and nasopharynx look normal. Mar., 1916. General health excellent. No recurrence tbc. glands on either side. Lungs clear on perc. and ausc. Oct., 1916. Temperature 99.4° F. Weight 99½ pounds. Impaired percussion note at both apices; no râles (Phipps Dispensary). X-ray report: En- larged mediastinal glands. Skin test O. T. positive. Nose and throat normal. Cervical glands barely palpable.
heart: Normal. ngs: Clear on perc. and ausc. rine: Normal. o general glandular enlargement.	98	July, 1915. Chronic tonsillitis. Chronic catarrhal otitis media. Mouth- breather.	None.	Nov., 1915. Glands on right side neck barely palpable; those at angle jaw on left are larger than at operation; not matted together; hard; not adherent to skin. Hearing improved. Throat and nasopharynx: Normal. Oct., 1916. Health same as before operation. Glands: Numerous ½ to 1 cm. in diameter at edge of jaw on both sides. Throat normal. Thinks hear- ing is worse. Examination of lungs (Phipps Dispensary); impaired per- cussion note above and below the clavicles. Skin O. T. +.

TABLE I.—SUMMARY OF CASES OF TUBERCULOSIS OF THE TONSILS OR ADENOIDS
III. CASES BETWEEN 11 AND 15 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	Special Examination. Tonsils, Adenoids, Teeth, Nose, Ears.	Microscopical Examination.			Glands. Size, Situation, Character.	History.
					Tbc. R. Tonsil.	Tbc. L. Tonsil.	Tbc. Adenoids.		
T. R. 38358. Male. 27.	C	14	School.	Tonsils: Small; embedded; adherent to pillars. Adenoids: Very small amount. Teeth: Carious. Ears: Normal. Nose: Normal.	0	0	+	Slightly enlarged at angle jaw and in posterior triangle on each side. Measure about 1½ cm. in diameter. Discrete, mobile, hard.	Frequent tonsillitis. No chronic cough; night-sweats or loss of weight.
A. D. 38539. Male. 28.	W	13	School.	Tonsils: Enlarged; adherent to pillars. Adenoids: Small amount. Ears: Chronic catarrhal otitis media. Teeth: Carious. Nose: Deflected septum to left.	+	+	0	Enlarged at angle jaw on each side; measure 2 x 3 cm. Hard, discrete, movable, not tender. Just palpable in posterior triangles.	Frequent sore throat, especially during past year. No cough or other symptoms of Tbc.
O. M. 38651. Female. 29.	W	11	School.	Tonsils: Much enlarged. Adenoids: Large mass; mouth-breather. Ears: Not infected. Nose: No sinus infection. Teeth: Good.	0	+	0	At angle jaw on each side measure about 2 cm. in diameter. Discrete, hard, movable. Smaller glands in posterior triangles and along sternomastoid. Scar of previous operation for tbc. glands neck on left.	Frequent tonsillitis, colds and difficulty in breathing through nose. No cough or other symptoms of Tbc.

IV. CASES BETWEEN 16 AND 25 YEARS OF AGE.

J. W. 30979. Male. 30.	W	19	Clerk.	Tonsils: Both enlarged; left, larger than right. Adenoids: Enlarged. Nose: Normal. Teeth: Good condition. Ears: Normal.	0	0	+	Enlarged at angle of jaw on both sides. Hard; discrete; not adherent to skin. Few small discrete glands in both posterior triangles.	For many years has had frequent attacks tonsillitis. Measles and scarlet fever. Hemoptysis once with an attack tonsillitis. Average weight 125 pounds. Has no cough; night-sweats; or loss of appetite.
E. K. 31381. Female. 31.	W	18	School.	Tonsils: Enlarged. Adenoids: Enlarged. Nose: Hypert. inf. turb. left, no sinus infection. Teeth: In bad condition. Ears: Chronic catarrhal otitis media.	+	+	+	Enlarged; soft; not fluctuant; discrete; tender on both sides neck at angle jaw. Few discrete, hard glands in posterior triangles.	Frequent sore throats. General health good. No symptoms of Tbc. noticed by patient. Comes to dispensary on account sore throats.
J. K. 32018. Male. 32.	W	25	Clerk.	Tonsils: Large; nodular; adherent to pillars. Adenoids: Large mass. Nose: Deviated septum; hypert. inf. turb. right. Ears: Normal. Teeth: Good.	+	+	0	Enlarged at angle of jaw on both sides, especially right. Hard; discrete; not adherent to skin. Few enlarged glands in posterior triangles.	Frequent attacks acute tonsillitis. Glands enlarged for 6 months. Grandmother died pulmonary Tbc. Had measles and pneumonia. No cough; night-sweats; loss weight. Slight elevation temperature evening for 6 mos.
J. I. 32119. Male. 33.	W	20	Tailor.	Tonsils: Much enlarged. Adenoids: Large; mouth-breather. Nose: Hypert. inf. turb. right. Ears: Chronic otitis media left.	0	0	+	Glands neck not enlarged.	No history of Tbc. in family; no cough. Chief complaint is frequent sore throats for past 3 years. Mouth-breather.
C. L. 32445. Female. 34.	W	18		Teeth: Poor. Tonsils: Right much enlarged; left small. Adenoids: Very small amount. Teeth: Excellent. Nose: Normal. Ears: Normal.	+	0	0	Glands neck not enlarged. Numerous hard, discrete glands in posterior triangles.	No history Tbc. in family. Always delicate. Measles, whooping cough, diphtheria. Has not been well since "grippe" 5 years ago. Enlargement thyroid noted 3 years ago. Frequent headaches and attacks of tonsillitis. Albumin discovered in urine 15 months ago.
M. B. 33265. Female. 35.	W	19	School.	Tonsils: Not enlarged; densely adherent to pillars. Adenoids: Small amount. Teeth: Excellent. Nose: Normal; sinuses clear. Ears: Normal.	0	+	0	Mass of glands measuring 3 x 8 cm. at angle of jaw on left. Involves both anterior and posterior triangles. Has had a discharging sinus on left side neck for 5 months. Typical tbc. glands.	No history Tbc. in family. Has been away to school for several years. Two attacks of tonsillitis during past 2 years. Has lost 20 pounds; poor appetite; always tired.
E. S. 33532. Male. 36.	W	24	Student.	Tonsils: Not enlarged; densely adherent. Adenoids: Very small amount. Teeth: Good. Nose: Hypert. inf. turbinates; mouth-breather. Ears: Normal. Has a chronic pharyngitis.	+	0	No tissue removed at opn.	Glands neck not enlarged. Few palpable glands in all triangles.	No history Tbc. in family. Chief complaint is frequent colds; hoarseness; tendency to clear throat. Diphtheria at age of 2½ years.
M. G. 34595. Female. 37.	C	22	Housework.	Tonsils: Not enlarged; adherent. Teeth: Good. Adenoids: Small amount. Nose: Normal. Ears: Normal.	0	+	+	Mass glands at angle jaw on right measuring 5 x 8 cm.; marked periadenitis; fluctuant. Typical tbc. glands. Glands on left not enlarged; in posterior triangles not enlarged.	No history of Tbc. in family. No illness except mumps in childhood. Swelling at angle right jaw first noted 3 years ago. Intermittent increase and decrease in size of gland with every coryza and tonsillitis. Has had no fever. Frequent attacks of tonsillitis and quinsy.
L. B. 34699. Female. 38.	W	19	Student.	Tonsils: Right larger than left; both adherent to pillars. Adenoids: Very small amount. Nose: Hypert. inf. turb. right. Teeth: Excellent. Nose: Normal.	0	+	No tissue removed at opn.	Measure 5 x 8 cm. at angle of jaw on right; also enlarged at angle of jaw on left. Hard, movable, not adherent to skin.	Had septic sore throat about one year ago; was then at school in Boston. Enlarged glands neck first appeared at this time. With each cold or sore throat they increase in size, then subside. No history Tbc. in family. Has frequent headaches; tires easily.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.—Continued.

General Physical Examination.	Temp. (Mouth) on Day Before Operation. ° F.	Date and Indication for Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Heart: Normal. Lungs: Clear on perc. and ausc. Spleen: Not palpable. Thyroid: Normal.	97.6	Nov., 1915. Chronic tonsillitis. Cervical adenitis. (Extraction carious teeth.)	None.	Oct., 1916. General health good. Has gained in weight. No sore throat since operation. Cervical glands just palpable. Marked lymphoid hyperplasia on posterior wall pharynx, otherwise nose, ears and throat are normal.
Heart: Normal. Lungs: Clear. Spleen: Not palpable. Thyroid: Normal. W. B. C.: 12,900. Hb.: 90%.	99	Dec., 1915. Chronic tonsillitis. Cervical adenitis. (Extraction carious teeth.)	None.	Sept., 1916. General health excellent. Gland at angle jaw on left same as at operation; is barely palpable on right. Glands in posterior triangles are slightly larger than at operation. Throat looks normal aside from lymphoid hyperplasia on pharynx wall. Tbc. skin test +. Temperature 99.6° F. Lungs clear on perc. and ausc. Is receiving tuberculin injections for tbc. cervical adenitis.
No general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: Normal. Spleen: Not palpable. General glandular enlargement. Thyroid: Normal. Ricket: Positive. Calmette 1%; negative.	99.1	Jan., 1916. Chronic tonsillitis. Mouth-breather. Tbc. glands neck. (Has had two operations for removal tbc. glands neck; last 2 years ago.)	None.	Sept., 1916. Recurrence tuberculous glands neck. General condition not improved. Suspicious involvement of right apex on physical examination and X-ray. No rales. Is getting tuberculin injections for the tuberculous glands. Throat normal. No glandular enlargement except two small shotty nodules along the scar at angle of left jaw.

IV. CASES BETWEEN 16 AND 25 YEARS OF AGE.

No general glandular enlargement. Lungs: Percussion note left apex impaired; a few rales after coughing. Heart: Normal. Liver and spleen not palpable. Kidneys: Normal. W. B. C.: 12,000. Hb.: 85%.	98-99	Nov., 1912. Frequent attacks tonsillitis. Enlarged cervical glands.	None.	Feb., 1916 (over 3 years after operation). General health has been excellent since operation. Works regularly. No cough or other symptoms of tuberculosis. Glands not palpable at angle of jaws. Throat normal.
No general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: Normal. Thyroid: Normal.	99	Jan., 1913. Frequent attacks tonsillitis. Enlarged cervical glands. (Referred to dentist.)	None.	Aug., 1915 (over 2½ years after operation). No palpable glands at angle of jaw on right; measures about ½ cm. in diameter at angle jaw on left. Barely palpable in posterior triangles. General health good; no sore throats since operation. Ears: Improved. Lungs clear.
Lungs: No physical signs. X-ray diagnosis: Old tbc. process at right apex and base. Heart: Normal. Thyroid: Normal.	99	May, 1913. Frequent attacks tonsillitis. Enlarged cervical glands. (Nasal operation also done.)	None.	Dec., 1915 (over 1½ years after operation). General health better than ever before; has gained weight; temperature and pulse normal for past year. Has been working regularly since operation.
Lungs: Clear on perc. and ausc. Heart: Normal. Thyroid: Normal.	97.6	May, 1913. Frequent attacks tonsillitis. Mouth-breathing. Chronic otitis media left. (Nasal operation also.)	None.	Oct., 1915 (2½ years after operation). No palpable glands. General health much improved since tonsillectomy. Breathes normally through nose. Throat looks normal; nasopharynx normal. Discharge from ear has stopped; hearing good.
Enlarged thyroid; exophthalmos; Von Graefe positive. Heart slightly enlarged to left. Blood pressure 112-130. Albumin, casts and blood in urine. Lungs: Normal. Clinical diagnosis: Chronic nephritis; chronic tonsillitis.	98	July, 1913. Frequent attacks tonsillitis. Chronic nephritis. Hyperthyroidism.	None.	Oct., 1915. Not improved. Had uræmia in summer of 1915. No evidence of tuberculosis of lungs or kidneys. Has been under constant treatment for nephritis. No colds or sore throat since tonsillectomy. Aug., 1916. No symptoms of tuberculosis in glands neck, lungs or kidneys. Still has albumin, hyaline and granular casts.
No general glandular enlargement. Lungs: Impairment of percussion note at right apex; also of expansion on right. X-ray: Shows evidence of old lesion on right. No tbc. bacilli in sputum. Never any cough or night-sweats. Calmette 1% positive. Heart and urine: Normal. W. B. C.: 10,000. Hb.: 76%.	98.6	Nov., 1913. Tbc. glands neck left. Chronic tonsillitis. (Local curettage of sinus on left side neck.)	None.	Nov., 1914. Sinus healed 6 months after tonsillectomy; mass of glands on left much smaller. Has gained 12 pounds. Has had no colds or sore throats since operation. Dec., 1915. No palpable enlarged glands on left side neck. No colds since operation. Is still under weight about 15 pounds. June, 1916. After a coryza and pharyngitis glands left side neck again enlarged; sinus reopened. Excision glands neck. Lungs as before.
No general glandular enlargement. Lungs: Normal on perc. and ausc. Heart: Normal. Thyroid: Normal.	98	Dec., 1913. Frequent colds. Chronic tonsillitis. Frequent attacks laryngitis. (Nasal operation also.)	None.	Dec., 1915 (2 years after operation). Has been studying in post-graduate work since operation; no symptoms of pulmonary or glandular Tbc. General health good. Lungs normal.
No general glandular enlargement. Lungs: Normal on perc. and ausc. Heart: Systolic murmur transmitted to axilla and back. Thyroid: Trace albumin. W. B. C.; no casts.	98.6	May, 1914. Tbc. glands neck right. Frequent attacks tonsillitis. Mitral insufficiency. (Excision tbc. glands neck on right side.)	None.	Feb., 1916 (nearly 2 years after operation). Had an attack of pleurisy in Dec., 1915. Two enlarged glands (tuberculous) at angle of jaw on left, and a recurrence about mid-way the sternomastoid on the right. Throat looks normal; nasopharynx normal; nose and ears normal.
No general glandular enlargement. Lungs: Normal on perc. and ausc. Heart: Normal. Kidneys: Normal.	99.2	June, 1914. Enlarged glands neck. History tonsillitis.	None.	Feb., 1916. Glands at angle of jaw on left are not palpable; still enlarged at angle of jaw on right, measures 2 x 3 cm. General health good. Lungs clear on perc. and ausc. Temperature normal.

TABLE I.—SUMMARY OF CASES OF TUBERCULOSIS OF THE TONSILS OR ADENOIDS
IV. CASES BETWEEN 16 AND 25 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	Special Examination. Tonsils, Adenoids, Teeth, Nose, Ears.	Microscopical Examination.			Glands. Size, Situation, Character.	History.
					Tbc. R. Tonsil.	Tbc. L. Tonsil.	Tbc. Adenoids.		
N. S. 35504. Female. 39.	W	23	Factory work.	Tonsils: Small; adherent to pillars, especially right. Adenoids: Very small amount. Teeth: Carious; alveolar infections. Nose: Normal. Ears: Normal.	+	0	0	Mass of glands at angle jaw on right; fluctuate; not tender; marked periadenitis. Definitely enlarged, hard, discrete glands on left and in both posterior triangles.	Enlarged glands at angle jaw on right first noted 4 months ago following typhoid fever. Never pained. Have gradually increased in size. No history of Tbc. in family. No history tonsillitis no cough.
H. C. 36205. Female. 40.	C	18	Maid.	Tonsils: Slightly enlarged; adherent to pillars. Adenoids: Not enlarged. Teeth: Carious. Nose: Normal. Ears: Normal.	0	+	0	Glands of neck not enlarged. Few palpable glands in submaxillary triangle; due to teeth.	Chief complaint is pain and stiffness of joints. Began about one month after attack acute tonsillitis in July, 1914. Since this time has walked with cane. Also shortness of breath on exertion. Frequent attacks tonsillitis. Has been in hospital on two previous occasions for treatment of joints. Attacks "fluttering of heart."
F. W. 38659. Female. 41.	C	19	Maid.	Tonsils: Right larger than left. Both embedded and adherent to pillars. Adenoids: Enlarged. Teeth: Pyorrhœa; caries. Ears: Chronic catarrhal otitis media. Nose: Hypert. inf. turb. Tonsils: Right larger than left; both embedded and adherent to pillars. Adenoids: Enlarged. Teeth: Caries. Ears: Normal. Nose: Hypert. middle and inf. turbinates.	0	+	+	Mass glands angle jaw left 6 x 4 cm.; matted together; fluctuate. Tbc. glands, right, have been removed.	Frequent attacks tonsillitis. Give no history of cough, sweating at night or loss of weight. Tbc. glands have been removed on right; recently glands on left have rapidly enlarged. No history pleurisy.
A. H. 38740. Female. 42.	W	22	Factory.	Tonsils: Right larger than left; both embedded and adherent to pillars. Adenoids: Enlarged. Teeth: Caries. Ears: Normal. Nose: Hypert. middle and inf. turbinates.	0	0	+	Tbc. glands neck on right removed 5 years ago. At present glands at angle jaw on each side 1 x 2 cm. in diameter; slightly matted together; not adherent to skin; hard.	Frequent tonsillitis. History night sweats, but no chronic cough. Glands neck at times become greatly enlarged and then almost completely disappear.
F. W. 31348. Male. 43.	W	29	Manufacturer.	Tonsils: Enlarged; densely adherent to pillars. Adenoids: Enlarged. Nose: Hypert. inf. turb. left. Ears: Normal. Teeth: Good. Marked iritis.	0	0	+	Has had two operations for tbc. glands neck. At present recurrence in anterior triangle on left, and posterior triangle on right. On left mass at angle jaw typical tbc. glands.	Onset enlarged glands about 5 years ago. Operation on right 4 years ago; on left 3½ years ago. For past 3 months has had double iritis. No symptoms of pulmonary lesion at present. Mother died Tbc. when patient was 4 years of age. Had right pleural effusion at 14 years of age. Hay fever for years. Frequent attacks tonsillitis.
J. M. 34742. Female. 44.	W	27	Housework.	Tonsils: Not enlarged; adherent to pillars. Adenoids: Not enlarged. Ears: Normal. Nose: Hypert. inf. turb. Teeth: Good.	+	+	0	Enlarged glands at angle of jaw on both sides. Not adherent; freely movable; measure 2 x 3 cm. on both sides.	No history of Tbc. in family. Chief complaint is frequent sore throats; almost constantly for past 3 months. Had not noticed enlarged glands neck. General health good. No cough.
L. R. 35203. Male. 45.	W	31	Merchant.	Tonsils: Both enlarged; left beyond mid-line. Adenoids: Large mass. Ears: Normal. Teeth: Good. Nose: Normal.	0	+	0	Very stout man. No glands palpable.	No history Tbc. in family. Measles, mumps, pertussis, varicella, typhoid fever. Chief complaint is: Chronic hacking cough; febrile attacks at irregular intervals; digestive disturbances; and rheumatism. Frequent attacks tonsillitis.
O. S. 35291. Male. 46.	W	34	Laborer.	Tonsils: Slightly enlarged; adherent; chronically infected. Adenoids: Small amount. Teeth: Pyorrhœa. Ears: Normal. Nose: Hypert. inf. turbinates; deflected septum.	+	+	0	A chain of slightly enlarged tender glands in both anterior and posterior triangles. At angles of jaw measure 3 x 2 cm.; no periadenitis; movable.	No history of Tbc. in family. Complains of nasal obstruction; catarrhal discharge into throat; almost constant sore throat for past 2 months. Frequent attacks tonsillitis. Frequent attacks laryngitis.

TABLE II.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR INFECTIOUS ARTHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
G. B. 29157. Female.	W	26	Nurse.	Tonsillitis every winter for several years. Complaints of stiffness in practically all joints, but elbows and ankles are particularly stiff and painful. Onset joint trouble insidious; no history of swelling or redness of joints. This was history given in 1912. In 1914 had severe attack tonsillitis with albumin and blood in urine; flare up of arthritis in all joints.	None.	Tonsils: Enlarged; adherent to pillars. Nose: Normal. Sinuses: Not infected. Ears: Normal. Nasopharynx: Small amount adenoid tissue; chronically infected. Teeth: Good. Cervical glands: Enlarged at angles jaw and in posterior triangles. Tonsils: Enlarged. Adenoids: Small. Sinuses: Clear. Teeth: Good. Cervical glands: Enlarged at angles jaw. Tonsils: Slightly enlarged; very adherent to pillars. Nose: Normal aside from hypert. inf. turb. Ears: Normal. Sinuses: Not infected. Teeth: Good. Nasopharynx: Chronically infected; discharge. Cervical glands: Enlarged; tender.	98.6
F. N. 29950. Male.	W	24	Farmer.	No history tonsillitis. Onset 1½ year ago left foot, ankle, right hip. Bony exostosis on os calcis left.	None.		
M. B. 29965. Female.	W	25	Nurse.	Frequent tonsillitis, but without constitutional symptoms until last attack 1 month ago; this was followed by stiffness and pain in both knees, and the artic. of jaw on right. Has difficulty in walking or eating. Onset of joint symptoms about 1 week after tonsillitis.	None.		99

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

IV. CASES BETWEEN 16 AND 25 YEARS OF AGE.—Continued.

General Physical Examination. Tuberculin Test.	Temp. (Mouth) on Day Before Operation. ° F.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
No general glandular enlargement. Lungs: Normal on perc. and ausc. Heart: Normal. Urine: Normal. Calmette 1% positive. W. B. C.: 12,000. Hb.: 92%.	98	Oct., 1914. Tbc. glands neck right. (Incision and curettage tbc. glands on right.) Tuberculin treatment advised. Referred to dentist.	None.	July, 1915 (9 months after operation). Has not been returning for tuberculin treatment. Large mass tbc. glands on right side neck discharging in two places. On the left only one small gland is palpable. Teeth poor; has not been to dental clinic. Throat looks normal with the exception of a granular pharyngitis. Lungs: Slight impairment at right apex; few râles after coughing. X-ray chest (30904) shows marked infiltration of both lungs; shadow at right of sternum, possibly enlarged glands.
Lungs: Clear on perc. and ausc. Heart: Enlarged to left; def. mitral insufficiency. W. B. C.: 10,700. Hb.: 79%. Urine: Normal.	98.6	Jan., 1915. Infectious arthritis. Mitral insufficiency.	None.	June, 1915 (6 months after operation). No symptoms of Tbc. Glands not enlarged. Lungs clear on perc. and ausc. Temperature normal. The joints gradually improved, and for two months have been normal. Throat looks normal. Pulse regular; heart measures 11.5 cm. to left and 4 cm. to right. Definite mitral insufficiency. Liver not enlarged. No longer has attacks of tachycardia.
General glandular enlargement. Heart: Normal. Lungs: Thickened pleura; sputum negative. Urine: Normal. Wassermann: Positive. Calmette 1% negative. Calmette 5% doubtful.	99.1	Dec., 1915. Chronic tonsillitis. Cervical adenitis Tbc. (Extraction carious teeth. Treatment for lues.)	None.	Aug., 1916. General condition poor. Now evidence of active tuberculosis at left apex. Sinus just above clavicle on left from mass of tuberculous glands. Wassermann still positive. Temperature 98° F.
General glandular enlargement. Heart: Normal. Lungs: Clear on perc. and ausc. Urine: Normal.	98.9	Jan., 1916. Chronic tonsillitis. Cervical adenitis. (Extraction carious teeth.)	None.	Sept., 1916. General health good. Temperature 98.7° F.; pulse 88; weight 135 pounds. Is 3 months pregnant. Cervical glands smaller than at time of operation; hard, freely movable. Lungs clear on physical examination. Skin test positive. At present has an acute antrum infection on right.
No general glandular enlargement. Lungs: Impaired percussion note over right lower back; no râles. X-ray: Thickened pleura right upper lobe. Infiltration both lungs. Tbc. skin test: Positive. Heart: Normal. Kidneys: Normal.	99	Jan., 1913. Tbc. glands neck. Recurrent after operation. (Incision and drainage tbc. abscess neck left.)	None.	July, 1913. Glands on left again enlarged and now discharging. One eye still inflamed. Has been taking tuberculin treatment. Jan., 1916. Glands on left almost entirely disappeared; on right are barely palpable. Eyes not normal, but much improved. Still takes occasional course of tuberculin.
No general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: Normal. Urine: Normal. Skin test: Positive. Calmette: Positive.	99.2	June, 1914. Frequent attacks tonsillitis. Enlarged cervical glands. (Nasal operation also.)	None.	Nov., 1914. General health good; no cough; no sore throat since operation. Glands neck not palpable on either side. Dec., 1914. Lungs: Slight impairment at right apex; few râles after coughing. General health good. Temperature normal. Is working regularly. Tbc. skin test positive; Calmette 1% positive. Throat and nasopharynx look normal. July, 1916. General health good during past 2 years; working regularly. No sore throats. There is a solitary gland at angle of jaw on right measuring 3 x 4 cm.; hard, movable, not tender. Has come gradually during past 7 or 8 months. Condition of lungs unchanged. Temperature normal. To enter hospital for removal enlarged gland on right. Oct., 1916. Caseous glands at angle jaw on right removed. To have tuberculin treatment.
Lungs: Clear on perc. and ausc. Heart: Normal. Urine: Normal.	99	Sept., 1914. Frequent attacks tonsillitis. Infectious arthritis. (Removal pigmented mole on chest.)	None.	Jan., 1916. In perfect health. Since discovery of tbc. tonsils has had repeated examinations of lungs and sputum; always negative. No palpable glands. No febrile attacks and no arthritis during past year. Temperature normal. Sept., 1916. No glandular enlargement. No symptoms of pulmonary or glandular tuberculosis. General health excellent.
Lungs: Clear on perc. and ausc. Heart: Normal. Urine: Normal. No general glandular enlargement.	99	Sept., 1914. Enlarged cervical glands. Frequent tonsillitis. Frequent laryngitis. (Nasal operation also.) (Referred to dentist.)	None.	Nov., 1915 (over 1 year after operation). General health excellent. No sore throat or laryngitis since operation. Teeth are in good condition. Glands neck barely palpable on both sides; not tender. Throat, nasopharynx and nose look normal. Lungs: No definite changes on physical examination. Oct., 1916. Has a definite pulmonary tuberculosis; sent to a sanatorium for treatment. Throat looks normal. Glands: Just palpable at angle jaw.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
No general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: Normal. Urine: (in 1912), normal; (in 1914), albumin; blood; no casts. Joints: Periarticular thickening; no redness; no fluid in capsule. X-ray: Only periarticular changes.	Sept., 1915. Frequent tonsillitis. Arthritis infections. Renal lesion. (Was first admitted in Jan., 1912, complaining of arthritis; refused operation at this time.)	None.	July, 1916. The stiffness and pain in joints has all cleared up; had one severe coryza and pharyngitis last winter without any associated joint symptoms. Urine: Normal.
General glandular enlargement. Heart and lungs: Normal. Secondary anaemia; no leucocytosis. W. B. C.: 5500. Hb.: 75%.	May, 1912. Chronic tonsillitis. Arthritis.	None.	June, 1915. Writes that joints began to improve after tonsil operation and "for the past 2 years have been normal."
Slight general glandular enlargement. Lungs: Normal. Heart: Normal. Urine: Normal. Joints: No redness; no fluid; periarticular infiltration.	May, 1912. Frequent tonsillitis. Arthritis infections. (Nasal operation also.)	None.	Feb., 1916 (nearly 4 years since tonsillectomy). No joint symptoms of any kind for the past 3 years. General health excellent. Has had only one severe coryza in past 4 years. Cervical glands not palpable on either side; no general glandular enlargement.

TABLE II.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR INFECTIOUS ARTHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
S. D. 29998. Female.	W	35	Housewife.	Frequent attacks tonsillitis since childhood, but no arthritis until 2 months ago. Onset with sore throat, fever, chill, anorexia, constipation and polyarthritis.	None.	Tonsils: Very large; crypts filled with mucopurulent material. Nose: Normal. Sinuses not infected. Ears: Normal. Teeth: Carious; pyorrhea. Nasopharynx: Small amount adenoids. Cervical glands: Enlarged; tender.	100
H. D. 31131. Male.	W	23	Student.	History frequent sore throats; never any joint symptoms till Oct., 1912. Followed severe tonsillitis at this time with stiffness in all joints; the shoulders, knees and feet were more involved than other joints. These joint symptoms first came on about two weeks after tonsillitis; slowly subsided. In Dec., 1912, had very acute attack polyarthritis; was unable to move without pain. Temperature 99-103°.	None.	Tonsils: Enlarged; adherent to pillars. Teeth: Good condition. Nose: Normal; no sinus infection. Ears: Normal. Nasopharynx: Small amount adenoids; chronically infected. Cervical glands: Enlarged; soft; tender in both anterior and posterior triangles.	98.6
K. K. 31862. Male.	W	31	Golf instructor.	After getting wet about one year ago had first attack tonsillitis that he remembers since childhood. Following this had pain and stiffness in shoulders. For past 6 months almost constant sore throat; shoulders and fingers now very stiff and painful; other joints not involved. Gonorrhea 4 months ago; was treated.	None.	Tonsils: Small; adherent to pillars; much scar tissue. Teeth: Poor; many carious. Nose: Normal; sinuses not infected. Nasopharynx: Chronically infected adenoids; discharge. Ears: Normal. Cervical glands: Enlarged in anterior and posterior triangles.	98.6
L. C. 31970. Female.	W	37	Housewife.	Sore throats or colds are infrequent. Onset polyarthritis 7 or 8 weeks ago; pain and swelling, but no redness, in knees, shoulders, wrists, elbows and fingers of both hands. Thinks she has had no fever. Since onset arthritis has had an attack tonsillitis. Frontal headache attacks for years. Discharge in nasopharynx for years.	None.	Tonsils: Enlarged; adherent; purulent material in some crypts. Nose: Hypert. both inf. and left mid. turb.; large septal spur left. Ethmoiditis. Ears: Chronic catarrhal otitis media double. Teeth: Many carious. Nasopharynx: Chronically infected; discharge from nose. Cervical glands: Enlarged on right; just palpable in other triangles.	98.2
C. O. 32697. Male.	W	6		Frequent sore throat. A diffuse erythematous rash for past 6 months. Pain and stiffness in all joints; never any joint swelling or redness. Frequent elevation of temperature to 103.	None.	Tonsils: Large; adherent. Nose: Discharge due to adenoids; otherwise normal. X-ray: Sinuses clear. Ears: Normal. Nasopharynx: Small amount adenoid; infected; chronic discharge. Teeth: Carious.	98.2
C. H. 32981. Male.	W	27	Blacksmith.	Infrequent sore throat and coryza. Onset 1 year ago with pain in left ankle; then became swollen. Other joints were successively involved, walks with difficulty. Unable to work. No digestive disturbances. No history lues or tripper.	None.	Cervical glands: Enlarged in all triangles. Tonsils: Small; adherent; probably infected secondarily by teeth. Nose: Hypert. inf. turb.; no sinus infection. Teeth—X-ray: Abscess at root wisdom tooth. Extensive pyorrhea. Nasopharynx: Small amount adenoid tissue. Ears: Normal. Cervical glands: Barely palpable.	99
U. P. 33149. Female.	W	13	School.	Frequent tonsillitis; nasal discharge. Stiffness of cervical and dorsal spine, hips, knees, fingers. Onset gradual several years ago. Was always frail and underdeveloped.	None.	Tonsils: Not enlarged; adherent to pillars. Nose: Discharge due to adenoids; no sinusitis. Ears: Drums intact; hearing good. Nasopharynx: Infected adenoids. Cervical glands: Enlarged; hard—in all triangles. Teeth: Good.	99
L. S. 33278. Female.	W	9	School.	No history sore throat or frequent colds. Not a mouth-breather. Swollen ankles, wrists, small joints fingers, and stiff spine for 18 months. Onset gradual. No fever. Marked muscular wasting.	Mitral insufficiency.	Tonsils: Small; embedded; adherent to pillars; chronic pharyngitis. Teeth: Fairly good; some caries. Ears: Normal. Nose: Discharge from adenoids; otherwise normal. Nasopharynx: Infected adenoids; discharge. Cervical glands: Very large in both anterior and posterior triangles.	
R. C. 33657. Female.	W	32	Housewife.	Repeated attacks quinsy. Arthritis began 4 years ago in arms following tonsillitis; involved knees, elbows and fingers 6 months later. Discharge in nasopharynx. Hay fever for 10 years.	None.	Tonsils: Enlarged; much scarring due to quinsies. Nose: Ethmoiditis and antrum infection left. Teeth: No root infection (X-ray). Nasopharynx: Chronically infected adenoids. Ears: Normal. Cervical glands: Enlarged at angles jaw; just palpable in posterior triangles.	99.3
R. H. 34716. Male.	W	29	Student.	Frequent attacks pharyngitis during latter part 1913. In Dec., 1913, had a severe attack tonsillitis; two weeks later first joint symptoms. First left ankle, then right ankle and fingers. Slight swelling; stiffness; pain on motion.	None.	Tonsils: Both small; densely adherent; fibrous; marked hypertrophic pharyngitis. Nose: Hypert. inf. turb. right; sinuses clear. Ears: Normal. Teeth: Good. Nasopharynx: Chronically infected adenoids; discharge. Cervical glands: Enlarged and tender in anterior triangles, especially on left; chain of slightly enlarged glands in each posterior triangle.	98.4
G. D. 34731. Female.	W	25	Housewife.	No severe tonsillitis attack for many years, but dryness, slight pain on swallowing and uncomfortable sensations in throat in A. M. for several months. For the past 6 months pain and stiffness in neck, both feet, the right shoulder and left ankle. Never swollen or red; painful to walk. Complains enlargement, and at times, painful glands in neck.	None.	Tonsils: Small; densely adherent to pillars. Nose: Septal deviation to right. Sinuses clear. Ears: Normal. Teeth: Good. Nasopharynx: Very small amount adenoid. Cervical glands: Enlarged at angle jaw on both sides; measure about 3 x 5 cm. Smaller glands in posterior triangles.	99

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
<p>Lungs: Normal. Heart: Soft systolic blow at apex; not transmitted to axilla; not enlarged. Blood culture: Negative. Urine: Normal. Joints: Fingers, knees, ankles swollen; not red; very painful on motion. Unable to walk for 2 months. General glandular enlargement. Lungs: Normal. Heart: Soft systolic blow at apex; not transmitted. Blood culture negative. Urine: Normal. Joints: Very painful on slight motion; knees are much swollen. (Was brought to hospital in ambulance.) Urethra: Normal. W. B. C.: 15,000. Hb.: 75%. Marked general glandular enlargement. Lungs: Normal. Heart: Normal. Urine: Normal. Urethra: Negative for gonococcus. Joints: No swelling; limitation of motion; pain on motion. X-ray: Only periarticular changes.</p> <p>No general glandular enlargement. Heart: Normal. Lungs: Impairment behind over left apex; no rales. Sputum: No Tbc. bacilli. Urine: Albumin trace; R. B. C. and W. B. C.; no casts. W. B. C.: 14,000. Hb.: 78%. No gonococci found. Marked general glandular enlargement. Heart and lungs: Normal. Urine: Normal. W. B. C.: 12,000. Spleen: Palpable. Culture from tonsils after excision—streptococcus.)</p> <p>No general glandular enlargement. Heart and lungs: Normal. Urine: Normal. W. B. C.: 4,600,000. W. B. C.: 7000. Hb.: 90%. No gonococci found. Wassermann: Negative.</p> <p>Mild general glandular enlargement. Heart and lungs: Normal. Urine: Normal. W. B. C.: 7000. Hb.: 95%. No urethritis. Joints: X-ray shows some new bone formation d. spine, and around affected joints. Weight: 50 pounds. Marked general glandular enlargement. Spleen palpable—enlarged. Lungs: Clear on perc. and ausc. Urine: Normal. Culture from tonsils after removal—staphylococci.)</p> <p>Hands in groin and axillæ enlarged. Heart and lungs: Normal. Urine: Normal. No urethritis. W. B. C.: 8000. Hb.: 90%. Wassermann: Negative.</p> <p>Mild general glandular enlargement. Heart and lungs: Normal. Urine: Normal. Wassermann: Negative. No urethritis.</p> <p>General glandular enlargement. Heart and lungs: Normal. Urine: Normal. Wassermann: Negative. No urethritis. Digestive tract normal, aside from constipation.</p>	<p>June, 1912. Frequent tonsillitis. Arthritis, infectious. (Extraction carious teeth.)</p> <p>Dec., 1912. Frequent tonsillitis. Arthritis, infectious.</p> <p>April, 1913. Chronic tonsillitis. Chronic nasopharyngitis. Arthritis, infectious. (Referred to dentist.)</p> <p>April, 1913. Chronic tonsillitis. Infectious arthritis. Ethmoiditis. (Also nasal operation and referred to dentist.)</p> <p>Aug., 1913. Erythema multiforme. Pain and stiffness joints. Elevated temperature two or three times a week to 103° F. Frequent tonsillitis. (Extraction carious teeth.)</p> <p>Oct., 1913. Infectious arthritis. (Extraction abscessed tooth; referred for treatment pyorrhea; nasal operation.)</p> <p>Oct., 1913. Frequent tonsillitis. Cervical adenitis. Infectious arthritis.</p> <p>Nov., 1913. Infected tonsils. Infected adenoids. General adenitis. Arthritis.</p> <p>Jan., 1914. Chronic tonsillitis. Arthritis, infectious. (Nasal operation.)</p> <p>June, 1914. Chronic tonsillitis. Arthritis, infectious.</p> <p>June, 1914. Chronic tonsillitis. Arthritis, infectious.</p>	<p>None.</p> <p>Bleeding on 3d and again on 4th after operation.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p> <p>None.</p>	<p>Aug., 1915. After leaving hospital improvement was gradual. About 6 months after operation all joint symptoms had disappeared, and have never recurred. No sore throat since operation. General health good. Cervical glands not palpable on either side in anterior triangle; few small glands in posterior triangles. Teeth: In poor condition. Throat and nasopharynx look normal with exception of a chronic hypertrophic pharyngitis. Nose: Normal. Heart: Normal in size; sounds clear.</p> <p>Jan., 1913. Joints rapidly cleared up after leaving hospital. Can now walk without pain; still some stiffness and swelling. Dec., 1915 (3 years after operation). Joints have been normal for past 2½ years. Has had no sore throats. Glands neck, axillæ, groins, not enlarged. Throat looks normal aside from hypertrophic pharyngitis (smoking).</p> <p>May, 1913. No improvement in joint condition. Glands neck still enlarged. April, 1914. Recurrence of stiffness and pain in shoulders and fingers in Jan., 1914; cleared up after 3 wks; now normal. Before this attack joints had been normal for 6 months. Cervical glands not palpable. Teeth in good shape. June, 1915. Joints all perfectly normal for over a year. Has recently won the golf championship for Canada.</p> <p>Aug., 1915 (over 2 years after operation). The pain and stiffness in knees and shoulders have entirely cleared up; still has occasional swelling and stiffness of elbows. All other joints normal. No new joints were involved after the operation on tonsils and nose. The improvement in condition of joints was very gradual; no symptoms in knees and shoulders for 1 year. Glands: Not palpable in either anterior or posterior triangles. Teeth: In good condition. Throat: Normal; no pharyngitis; no discharge from nose. Nose: Good breathing space; no discharge; no polypi. Headaches much less frequent and less severe.</p> <p>Aug., 1915 (2 years after operation). History is that child has been entirely well since tonsillectomy. No recurrence of erythema, rheumatism, tonsillitis or elevation of temperature. Glands: Left anterior cervical triangle about ½ cm. in diameter; just felt in other triangles; just palpable in axillæ and groin. Spleen: Not palpable. Teeth: Several carious. Nose, ears, throat, all look normal.</p> <p>June, 1915. Since leaving hospital has had several acute attacks polyarthritis; new joints have become involved; spine stiff. Unable to work. Has had no colds or sore throats. X-ray teeth shows no abscesses at root; still has pyorrhea. Heart: Normal. Nov., 1916. Much improved since removal of all teeth about two years ago. Works regularly as machinist for past 1½ years. Good movement in all joints; no deformity. Still some swelling of one of small joints index finger left hand. Weight 144 pounds. Nose and throat look normal. Heart normal. June, 1915. Has gained over 50 pounds in weight. Joints much improved though still quite stiff. No new joints involved. Cervical glands not palpable. General health better than ever before.</p> <p>May, 1914. Joints improved; right hip has become involved. Glands neck, groin, axillæ, epitrochlears enlarged. Spleen palpable. June, 1915. No pain in any of joints at present; all stiff. Goes to school regularly for past year. Nose and throat look normal aside from hypertrophic pharyngitis. Glands still enlarged though smaller. Teeth carious. Nov., 1916. Joints still stiff at times. No new joints involved. Goes to school regularly.</p> <p>June, 1915. Reports no improvement in condition of joints. No new joints involved. No tonsillitis or colds since operation. Still some nasal discharge. (Advised another nasal operation for ethmoiditis.)</p> <p>Nov., 1915. General health much improved since removal of tonsils; weighs 15 pounds more than ever before. One attack laryngitis in Jan., 1915, but otherwise no sore throats or colds. After the operation the joints gradually improved, but it was 6 months before the stiffness entirely disappeared; since Jan., 1914, have been entirely normal. No new joints were ever involved after the tonsillectomy.</p> <p>July, 1915. General health much better during past year. No general glandular enlargement; cervical glands not palpable. Throat feels normal. All joints have been normal for about 8 or 9 months. Has gained 15 pounds in weight.</p>

TABLE II.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR INFECTIOUS ARTHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
R. S. 34733. Female.	W	27	Student.	Tonsillitis 2 years ago followed by arthritis in one knee and one elbow. No swelling but tenderness and stiffness. These joints have never entirely returned to normal. Worse following cold about 3 months ago.	None.	Tonsils: Small; adherent, particularly on rt. Nose: Normal; sinuses clear. Ears: Normal. Teeth: Good. Nasopharynx: Large mass adenoids. Cervical glands: Enlarged at angle jaw on right. Measure 3 x 5 cm. Slightly enlarged on left and in posterior triangles.	99
R. A. 34893. Female.	W	13	School.	Complains of almost constant "cold" in head, and frequent sore throat. Headache daily. For several months has had swelling, pain, stiffness in left ankle, right arm and shoulder, and fingers.	None.	Tonsils: Have been partially removed; remains covered with scar tissue. Nose: Marked septal deflection to right; evidence of ethmoiditis on right. Ears: Normal. Teeth: Very bad condition; carious; abscess. Nasopharynx: Small amount adenoids; chronically infected.	99.4
C. B. 35252. Female.	W	22	Student.	Sore throat and colds very infrequent. Arthritis at intervals all her life. After exposure to cold 6 months ago joints became much worse; ankles, knees, fingers are involved. Swollen, painful, never red. No history of fever. Onset arthritis insidious.	None.	Cervical glands: Much enlarged at angle jaw on both sides. Tonsils: Very small; fibrous; adherent to pillars. Nose: Hypert. inf. turb. causing obstruction. Sinuses not infected (X-ray). Ears: Normal. Teeth: X-ray shows abscess at root of upper and lower incisors. Nasopharynx: Discharge from nose posteriorly; chronic infection adenoids.	98.2
A. C. 35256. Female.	W	52	Cleaner.	Frequent sore throat since childhood; quinsy. Knees and ankles swollen and painful for 1 year. Unable to work most of time on account of difficulty in walking. Referred from Gynecological Department.	None.	Cervical glands: Enlarged (2 x 3 cm.) at angle jaw on right; just palpable in other triangles. Tonsils: Small, fibrous, adherent. Nose: Hypert. inf. turb.; otherwise normal. Teeth: All removed. Ears: Normal. Nasopharynx: Infected adenoids; discharge from posterior nares.	98
W. H. H. 35427. Male.	W	53	Lawyer.	History frequent tonsillitis all his life. Arthritis began in right knee 4 years ago; swelling; no redness; pain on walking. Joints always worse after every coryza. Since last tonsillitis 1 month ago the right shoulder is involved.	None.	Cervical glands: Not enlarged, but palpable in all triangles. Tonsils: Small, fibrous, densely adherent. Nose: Inf. turb. greatly hypert.; no sinus infection. Ears: Normal. Teeth: Extensive pyorrhea. Nasopharynx: Discharge from posterior nares.	98.4
M. K. 35836. Female.	W	23	Housewife.	Tonsillitis once or twice every winter for years; quinsy three times. For 3 years has had pain, stiffness, swelling of elbows, knees and ankles. No history rheumatic fever.	None.	Cervical glands: Enlarged and tender at angles jaw, especially on right. Neck is frequently stiff. Tonsils: Enlarged; much scar tissue. Nose: Normal. Teeth: Good. Ears: Normal. Nasopharynx: Small amount adenoid.	99.2
A. G. 33073. Female.	C	35	Cook.	Frequent tonsillitis. Almost constant sore throat for 2 months. Both shoulders stiff and painful. Unable to work.	None.	Cervical glands: Not enlarged but palpable at angles of jaws and posterior triangles. Tonsils: Embedded; small; adherent. Adenoids: Small; infected. Teeth: Good. Sinuses: Not infected.	98.2
W. S. 33814. Male.	W	29	Laborer.	Frequent tonsillitis for past 3 years; with each attack has pain and stiffness in practically all large joints. Is just recovering from an attack.	None.	Cervical glands: Slightly enlarged; tender. Tonsils: Left larger than right; both adherent. Adenoids: Small. Teeth: Good. Sinuses: Not infected.	98
H. C. 36143. Female.	W	16	Clerk.	Frequent tonsillitis. Arthritis began 1 year ago in knees and ankles; clears up and recurs with every cold. Severe attack 1 month ago.	None.	Cervical glands: Enlarged; especially left. Tonsils: Enlarged, both sides. Adenoids: Small; chronically infected. Teeth: Carious. Sinuses: Not infected.	99.2
L. C. 36637. Male.	W	11	School.	Tonsillitis frequent past 3 years. Arthritis for 2 years; the shoulders and knees involved. Arthritis always associated with sore throat. No chorea.	None.	Cervical glands: Enlarged and tender angles jaw. Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious. Sinuses: Not infected.	98.5
M. P. 36768. Female.	W	15	School.	Occasional sore throat; never severe. First came to Orthopedic Dispensary 1907 with arthritis in ankles and knees. Another attack in 1914, and a third attack about 1 month ago. Hands, shoulders, knees involved. Walks with difficulty. No other illness.	None.	Cervical glands: Enlarged angles jaw both sides. Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Good. Sinuses: Not infected.	98
A. W. 37245. Female.	C	25	Maid.	Referred from Orthopedic Department where she has been treated for infectious arthritis. Frequent tonsillitis since childhood. Wrists, fingers, back and knees involved. Frequent frontal headache.	Mitral insufficiency.	Cerv. glands: Slightly enlarged at angles jaw. Tonsils: Slightly enlarged; very adherent to pillars. Adenoids: Small; infected. Teeth: Carious. Sinuses: Not infected.	99
E. C. 37312. Female.	C	9	School.	Frequent tonsillitis with high fever. Swelling glands neck. Onset arthritis 2 years ago after sore throat; all joints in arms and hands were involved; fingers still stiff and painful. Recently knees involved.	None.	Cervical glands: Enlarged angles jaw. Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious. Sinuses: Not infected.	99
W. C. 37499. Male.	W	8		Frequent acute sore throats; constant "cold in head." Arthritis for over one year; knees and ankles swollen, stiff, painful. Walks with difficulty.	None.	Cervical glands: Size walnuts angles jaw. Ears: Chronic supp. otitis media. Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious. Sinuses: Not infected.	99
O. T. 37630. Male.	W	3		Unable to walk on account swelling and pain in ankles and knees. "Always worse after colds." Arthritis came on 2 weeks after tonsillitis.	None.	Cervical glands: Enlarged angles jaw. Tonsils: Slightly enlarged; adherent to pillars. Adenoids: Large mass. Teeth: Good. Sinuses: Not infected (X-ray).	99.6
						Cerv. glands: Slightly enlarged at angles jaw.	

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
No general glandular enlargement. Heart and lungs: Normal. Urine: Normal.	June, 1914. Chronic tonsillitis. Cervical adenitis right. Arthritis, infectious.	None.	June, 1915. Has had no pain or stiffness in joints during past 8 months. Skin is much clearer. General health improved. Had one slight "cold" last winter instead of the usual half dozen. Cervical glands not palpable on either side.
General glandular enlargement. Heart and lungs: Normal. Urine: Normal.	July, 1914. Chronic tonsillitis. (Tonsils have been partially removed.) Arthritis, infectious. Cervical adenitis. (Extraction carious teeth.)	None.	Jan., 1915. No change in arthritic condition; polypoid m. m. anterior end middle turb. rt.; discharge. Refuses operation on sinuses. July, 1915. Joints still stiff; right hip has become involved. Frequent headaches. Ethmoiditis right; discharge into nasopharynx. Cervical glands are not palpable in the anterior triangles; not enlarged in posterior triangles. Again refused nasal operation. Heart normal. Note.—The chronic tonsillitis in this case was probably secondary to the ethmoidal infection and the nasal operation should have been done first.
No general glandular enlargement. Heart and lungs: Negative. Urine: Normal. W. B. C.: 10,000. Hb.: 85%. No urethritis. Wassermann: Negative.	Sept., 1914. Chronic tonsillitis. Arthritis, infectious. (Nasal operation also.)	None.	Nov., 1914. All joint symptoms rapidly cleared up after leaving hospital; is at present entirely free from stiffness or pain. Feb., 1916. Recurrence of acute polyarthritis in Dec., 1914; not associated with cold or other trouble of any kind. All joints were involved in succession. Very slight if any fever. Heart normal. Has had osteopathic treatment. Spent several months at Hot Springs, Ark., and Mt. Clemens, Mich., without any benefit. At present in worse condition than ever before.
No general glandular enlargement. Heart and lungs: Normal. Urine: Normal. No urethritis. Wassermann: Negative.	Sept., 1914. Frequent tonsillitis. Arthritis, infectious.	None.	Oct., 1914. Joints rapidly improved after operation; for a few days were more swollen and painful than before, but at the end of a week the swelling and pain on motion rapidly disappeared. Can now walk and work without pain for first time in 6 months. Aug., 1915. All joints practically normal for a year; works regularly. Glands not palpable in neck. Nose and throat normal.
No general glandular enlargement. Heart, lungs: Normal. Urine: Normal. Blood pressure 175 mm. Hg. Wassermann: Negative. No urethritis. Circumference right knee 41½ cm. X-ray: Shows only periarticular changes; cartilage not injured.	Oct., 1914. Chronic tonsillitis. Arthritis, infectious. (Nasal operation also. Referred for treatment of pyorrhea.)	None.	Nov., 1914. Swelling knees slightly increased; very difficult to walk. Jan., 1915. No improvement in condition of joints. Cervical glands much smaller. Throat looks normal. Nose normal. June, 1915. Other joints becoming involved. Teeth have been treated. Throat normal. No gastro-intestinal symptoms. Aug., 1916. Much improved. Very little, if any swelling of knees, but "the stiffness and soreness of elbows and knees is felt very acutely during damp weather." Other joints normal. General health good.
Slight general glandular enlargement. Heart and lungs: Normal. Urine: Normal. No urethritis. Wassermann: Negative. R. B. C.: 4,900,000. W. B. C.: 10,700. Hb.: 60%.	Dec., 1914. Chronic tonsillitis. Arthritis, infectious.	None.	June, 1915. All joints are now normal for the first time in 3 years; no symptoms for past 4 months. Glands in anterior and posterior triangles are not palpable. Throat looks and feels normal. Sinuses clear on examination and X-ray. Has frequent headaches, which must be due to eyes. (Referred to oculist.)
No general glandular enlargement Heart and lungs: Clear. Wassermann: Negative. Urine: Normal.	Oct., 1913. Chronic tonsillitis. Arthritis.	None.	Oct., 1915. No trouble with joints for past 1½ years. Cervical glands; not palpable. Throat: Looks normal. Teeth: Good.
No general glandular enlargement. Heart and lungs: Clear. Urine: Normal. No urethritis. W. B. C.: 8600. Hb.: 85%. Heart and lungs: Clear. Urine: Clear. Gynecological examination: Negative.	Jan., 1914. Chronic tonsillitis. Arthritis. Jan., 1915. Chronic tonsillitis Arthritis.	None. None.	Sept., 1915. Joints normal since operation. No colds or sore throat since operation. Gained in weight. Cervical glands not palpable either side. Oct., 1915. Had one attack arthritis since operation; was in bed for several days. At present joints normal. Cervical glands not palpable. Throat: Looks normal.
Heart and lungs: Normal. Spleen: Not palpable. Urine: Normal.	April, 1915. Chronic tonsillitis. Arthritis.	None.	Nov., 1915. No symptoms of arthritis since operation. Cervical glands; Not palpable right; just felt left. Teeth: Good. No colds or sore throat since operation.
Heart and lungs: Normal. Urine: Clear.	April, 1915. Chronic tonsillitis. Arthritis.	None.	Jan., 1916. Joints all normal. Cervical glands: Not palpable. Throat: Normal aside from lymphoid hyperplasia on pharynx.
Heart: Enlarged, def. mitral lesion. Lungs: Clear on perc. and ausc. Liver: Not enlarged. Wassermann: Negative.	June, 1915. Chronic tonsillitis. Arthritis. (Extraction carious teeth.)	An acute flare-up of arthritis; joints swollen and painful; gradually cleared up.	July, 1915. All joints are normal subjectively and objectively. May, 1916. Joints normal since tonsillectomy. General health "better than for years." Cervical glands not palpable either side. Throat: Looks normal. Headaches very infrequent since operation.
Heart and lungs: Clear. Urine: Normal.	June, 1915. Chronic tonsillitis. Arthritis.	None.	Nov., 1915. Joints all normal. Ears: Normal; hearing good. Throat: Normal aside from lymphoid hyperplasia. Referred to dental department for treatment alveolar abscess. Nov., 1916. Joints normal. General health excellent.
Heart and lungs: Clear. Urine: Normal.	July, 1915. Chronic tonsillitis. Arthritis.	None.	Nov., 1915. Joints all normal subjectively and objectively for first time in a year. Teeth: Good. Throat: Looks normal. Cervical glands not palpable on either side.
Heart and lungs: Normal. No general glandular enlargement. Pirquet: Negative 48 hours. Urine: Negative.	Aug., 1915. Chronic tonsillitis. Arthritis.	None.	Nov., 1915. Joints all normal. Unable to examine nose and throat. General health excellent.

TABLE II.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR INFECTIOUS ARTHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
P. H. W. 34400. Male.	W	17	School.	No history tonsillitis but frequent pharyngitis. Scarlet fever 3 years ago. Tonsillitis 2 months ago; 2 weeks later involvement both hands, feet and knees.	None.	Tonsils: Small and densely adherent. Mucopurulent discharge in nasopharynx. Nose: Obstruction due to septal deviation; no sinus infection. Cervical glands: Enlarged at angles jaw.	99.5
H. B. P. 38448. Male.	W	37	M. D.	Constant backache for 2 years. No other joints involved. Frequent colds but no severe tonsillitis.	None.	Tonsils: Small, adherent; much scar tissue. Adenoids: Small, infected. Teeth: Poor condition. Nose: No sinus infection. Cervical glands: Markedly enlarged in posterior triangles.	99.2

TABLE III.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR MYALGIA

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
A. C. 31906. Female.	W	11	School.	Pains, stiffness, tenderness muscles both legs above knee; sometimes constant ache, like "toothache"; again paroxysms of shooting pain, particularly at night. Onset after tonsillitis about a year ago; getting worse. Mouth-breather. No history arthritis or chorea.	None.	Tonsils: Much enlarged; adherent to pillars. Nose: Discharge due to adenoids. No sinus infection. Ears: Normal. Teeth: Few carious areas. Nasopharynx: Large mass adenoids. Cervical glands: Much enlarged in all triangles.	98.6
A. W. 34712. Female.	W	23	Housewife.	Pain in arms, muscles of back and frequent "stiff" neck for the past 2 years. Onset following attack of tonsillitis 2 years ago; no sore throat since this attack. Glands neck enlarge at times, and become very tender. Digestive tract good condition.	None.	Tonsils: Much enlarged; adherent to pillars. Nose: Normal. Ears: Normal. Teeth: Good. Nasopharynx: Small amount adenoid. Cervical glands: Enlarged, tender at angle of jaws.	98.6
A. C. 34756. Female.	W	38	Nurse.	Soreness and stiffness of back, right arm, fingers, and right side neck at frequent intervals for past 2 years. No arthritis. Frequent sore throat for past 2 years. Has had only two attacks acute tonsillitis in past 2 years.	None.	Tonsils: Small; embedded; adherent to pillars. Nose: Hypert. inf. turbinates; otherwise normal. Ears: Normal. Teeth: Good. Nasopharynx: Small amount infected adenoids.	99
T. S. 36711. Male.	W	27	Lawyer.	Onset 2 years ago following toothache and exposure to cold. Pain, stiffness in left leg. Frequent cramps in muscles left thigh and calf. After a few months muscles of right leg and fingers of right hand involved. Extraction abscess tooth with temporary relief.	None.	Cervical glands: Slightly enlarged, tender. Tonsils: Enlarged; very adherent. Nose: Normal. Ears: Normal. Teeth: Opening into left antrum due to extraction of molar tooth; others good. Nasopharynx: Small amount adenoid. Cervical glands: Enlarged at angles jaw.	97.5

TABLE IV.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR RHEUMATOID ARTHRITIS

R. C. 29274. Male.	W	17	Cotton factory.	Tonsillitis frequent, last time 14 months ago. Arthritis began 8 months ago in fingers; other joints grad. involved. All large joints now involved. Lost 10 pounds in weight. Is a mouth-breather.	None.	Tonsils: Slightly enlarged; adherent to pillars. Nose: Practically normal; no sinus infection. Ears: Normal. Teeth: Good. Nasopharynx: Large mass adenoids; infected. Cervical glands: Enlarged; hard at angles jaw on both sides; also posterior triangles.	99
B. C. 29450. Female.	W	55	Housewife.	No history tonsillitis; colds infrequent. Onset arthritis 5 years ago. Arms, shoulders, elbows, knees, ankles all involved.	None.	Tonsils: Enlarged; large crypts filled with debris. Nose: Left side greatly hypert. inf. turb.; no evidence sinus infection. X-ray negative. Ears: Normal. Teeth: Abscess at root upper molar on right. Nasopharynx: Discharge from posterior nares; otherwise negative. Cervical glands: Measure 2 x 5 cm. at angle jaw on left; slightly enlarged in other triangles.	98.5
M. G. 29846. Female.	W	32	Housewife.	Quinsy 2 years ago; severe tonsillitis 4 months ago. Pain and stiffness spine for 14 years; recently much worse. After last tonsillitis shoulders and other joints involved for first time. Is entirely helpless; great pain on moving in bed.	None.	Tonsils: Enlarged; much scar tissue; crypts filled with debris at upper pole. Nose: Normal; sinuses clear (X-ray). Ears: Chronic supp. otitis media double for 4 months. Nasopharynx: Chronically infected adenoid; discharge from Eustachian tubes. Teeth: In poor condition. X-ray: No root infection. Cervical glands: Enlarged, tender, both sides.	97.8
N. G. 32290. Female.	W	41	Housewife.	For 10 or 15 years attacks of tonsillitis once or twice a year. Following each of these attacks there were some joint symptoms, and after a few an acute polyarthritis. Up to 3 years ago joints have always cleared up between the sore throats; since this time have been stiff and painful. Cervical and thoracic spine, fingers, shoulders, knees are now involved. Muscles wasted. Weight 40 pounds below normal.	None.	Tonsils: Small; adherent to pillars; marked chronic pharyngitis. Nose: Hypert. inf. turb.; otherwise normal. Teeth: Much dental work. X-ray: No root infection. Ears: Normal. Nasopharynx: Chronically infected; discharge. Cervical glands: Enlarged, hard, freely movable at angles jaw; also in posterior triangles.	98.8

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Heart and lungs: Normal. Has general glandular enlargement. Blood pressure 132 m. m. (Tycos). R. B. C.: 4,700,000. W. B. C.: 5400. Hb.: 75%. Urine: Tr. albumin; no casts. Wassermann: Negative.	July, 1914. Chronic tonsillitis. Arthritis. (Nasal operation also done.)	None.	Aug., 1916. Joints all normal. General health excellent for past 1½ years.
Heart and lungs: Normal. Urine: Normal. Wassermann: Negative. X-ray: Spine shows no bony changes.	Nov., 1915. Chronic tonsillitis. Infected adenoids. Spondylitis, infectious. (Re- ferred to dentist.)	None.	Aug., 1916. Back was worse for six weeks after tonsillectomy. Then began to improve. Has been perfectly well since April, 1916. Normal range of motion of spine. Working regularly for past 5 months. Has gained 35 pounds in weight.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Marked general glandular enlargement. Spleen: Large. Heart and lungs: Normal. Urine: Normal. W. B. C.: 9500. Hb.: 85%. No local swelling or redness of affected muscles.	April, 1913. Chronic tonsillitis. Cervical adenitis. Mouth-breather. Myalgia.	None.	May, 1913. Still has some stiffness and occasional pain in affected muscles. Mother says she is much better than at any time during preceding 6 months. Glands still enlarged in neck and axillæ, groins. Spleen palpable. Throat and nasopharynx look normal aside from a hypertrophic pharyn- gitis.
No general glandular enlargement. Spleen not palpable. Heart and lungs: Normal. Urine: Normal.	June, 1914. Chronic tonsillitis. Cervical adenitis. Myalgia.	None.	April, 1914. No muscular pain or stiffness for over a year. General health excellent. Glands neck not palpable. Still slight general glandular enlargement. Spleen not palpable. Feb., 1916. No recurrence of pain in arms; stiffness of neck or back for over one year. Throat looks normal. Glands in anterior triangle are not palpable; a few slightly enlarged glands felt in each posterior triangle. General health ex- cellent.
No general glandular enlargement. Heart and lungs: Normal. Urine: Normal.	June, 1914. Chronic tonsillitis. Myalgia.	None.	Jan., 1916. Entirely relieved of soreness and stiffness in arm, back, fingers, and neck. Throat looks normal aside from a hypertrophic pharyngitis. Cervical glands: Not palpable in anterior triangle; small, hard in posterior triangles.
No general glandular enlargement. Heart and lungs: Normal. Urine: Normal. Wassermann: Negative.	April, 1915. Chronic tonsillitis. Cervical adenitis. Myalgia.	None.	Jan., 1916. Entirely well. No recurrence of trouble for past year. Cervical glands not palpable.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

General glandular enlargement. Heart: Normal. Lungs: Bronchiectasis. Joints X-ray: Bony changes. Erosion of cartilage. Gastric analysis: Negative. W. B. C.: 8500. Hb.: 72%. No urethritis. Wassermann: Negative.	Feb., 1912. Chronic tonsillitis. Rheumatoid arthritis.	None.	June, 1915 (over 3 years after operation). Joints worse; spine involved. Has been in bed or wheel chair all the time since leaving hospital. Legs much retracted; muscles atrophied. Throat normal. No colds during past 3 years.
Slight general glandular enlargement. Heart: Not enlarged; soft systolic murmur, not transmitted. Lungs: Normal. Urine: Normal. Wassermann: Negative. Gynecological examination negative. X-ray joints show bony changes.	Mar., 1912. Enlarged tonsils. Enlarged cervi- cal glands at angle jaw left. Rheumatoid arthritis. (Referred to dentist.)	None.	June, 1915. No improvement in joints; walks with crutches. Baking affords some relief. Glands neck not palpable.
General glandular enlargement. Heart and lungs: Normal. Thyroid: Enlarged; tremor; pulse rapid. Urine: Clear. R. B. C.: 4,600,000. W. B. C.: 9200. Hb.: 80%.	May, 1912. Chronic tonsillitis. Chronic otitis media. Rheumatoid arthritis.	None.	June, 1915. No improvement in condition of spine; other joints have never cleared up. Still has great deal of pain which is relieved by atophan more than any other drug. Thyroid condition improved. Cervical glands barely palp- able. Has had no sore throat since operation. Ears ceased to discharge about 1 month after operation. Hearing good.
Slight general glandular enlargement. Heart and lungs: Normal. Urine: Trace albumin; no casts. W. B. C.: 7200. Hb.: 93%. X-ray joints shows overgrowth of bone, and some destruction of cartilage.	June, 1913. Chronic tonsillitis. History fre- quent sore throat with arthritis. Rheuma- toid arthritis.	None.	June, 1915. Marked improvement of joint condition. No new joints have become involved. Much less pain. Now has good motion of head, shoulders and arms but not to their normal extent. Muscles still quite weak. She can now "dress her own hair." Throat normal; no discharge from nasopharynx. Has had no "colds" since operation.

TABLE IV.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR RHEUMATOID ARTHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth) on Day Before Operation. ° F.
G. A. 34234. Male.	W	19	Clerk.	Stiff and painful back for 1 year; hips and knees involved for longer time. Back getting worse. Is mouth-breather. Infrequent sore throats. Referred from orthopedic clinic.	None.	Tonsils: Slightly enlarged; densely adherent to pillars. Teeth: Infected wisdom on left. Nose: Enlarged inf. and middle turb. left; clouding left antrum (X-ray). Ears: Normal. Nasopharynx: Large mass adenoids. Cervical glands: Enlarged; tender; hard; movable; in anterior and posterior triangles. Tonsils: Small; embedded; densely adherent to pillars. Teeth: Most have been removed; others good. Nose: No discharge; sinuses appear clear. Ears: Normal. Nasopharynx: Small amount infected adenoids. Cervical glands: Slightly enlarged at angle jaws and in posterior triangles.	99.8
J. D. 34293. Male.	W	48	Architect.	No history tonsillitis but discharge into throat due to infected sinuses. Onset arthritis 8 years ago with pain in back and abdomen; back grad. became stiff and painful. Other joints involved gradually. In May, 1913, fluid (250 cc.) removed from right knee; culture negative. Three months ago left knee involved. Sinus operation in 1913 without benefit.	None.	Tonsils: Small; densely adherent to pillars. Teeth: Pyorrhea; no root abscess (X-ray). Nose: No evidence of sinus infection. Ears: Normal. Nasopharynx: Chronically infected adenoids; discharge. Cervical glands: Enlarged at angle jaw, especially right.	99.6
G. M. 34480. Male.	W	29	Teacher.	Infrequent sore throats and coryza. Onset arthritis 2 years ago, involving hips, sacroiliac joints, fixation of ribs, right knee and ankle, both shoulders. No headache. No digestive disturbances.	None.	Tonsils: Small; embedded; adherent to pillars; chronic hypert. pharyngitis. Nose: No evidence of sinus infection. Ears: Chronic catarrhal otitis media double. Teeth: Pyorrhea; infection under crown. Nasopharynx: Chronically infected adenoids; discharge. Cervical glands: Markedly enlarged at angles jaw; painful on palpation. Enlarged in both posterior triangles.	98.6
L. W. 34531. Female.	W	51	Housewife.	Occasional tonsillitis since childhood; frequent coryza. Onset arthritis was insidious. At present walks only with crutches; contractures right leg particularly. Practically all large joints and many small joints involved.	None.	Tonsils: Small; embedded; adherent to pillars. Chronic pharyngitis. Teeth: Many carious; pyorrhea. Nose: Deflected septum to right; no sinus infection. Ears: Normal. Nasopharynx: Infected adenoids; discharge. Cervical glands: Not enlarged; just palpable at angle jaws and in posterior triangles.	99.8
L. H. 35026. Female.	W	46	Housewife.	Frequent tonsillitis during past 15 years. First noticed arthritis 8 years ago; gradually involved spine, hips, knees, shoulders, fingers. No digestive disturbances aside from constipation.	None.	Tonsils: Small; embedded; adherent to pillars. Chronic pharyngitis. Teeth: Many carious; pyorrhea. Nose: Deflected septum to right; no sinus infection. Ears: Normal. Nasopharynx: Infected adenoids; discharge. Cervical glands: Not enlarged; just palpable at angle jaws and in posterior triangles.	99.8

TABLE V.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR ACUTE RHEUMATIC FEVER

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination. Tonsils, Nose, Sinuses, Ears, Nasopharynx, Teeth, Cervical Glands.	Temp. (Mouth) on Day Before Operation. ° F.
A. H. 28956. Male.	W	10	School.	In 1907 acute tonsillitis followed by measles. In 1908 acute rheumatic fever with involvement of joints. In 1909 a second attack acute rheumatic fever with arthritis and chorea. In 1910 a third attack acute rheumatic fever. On present admission is just recovering from a fourth attack of rheumatic fever with arthritis and chorea. All attacks associated with tonsillitis.	Aortic insufficiency. Mitral insufficiency. Cardiac arrhythmia. Chorea.	Tonsils: Only slightly enlarged; densely adherent to the pillars. Nose: Normal. Sinuses: All seem clear. Ears: Normal. Nasopharynx: Chronically infected adenoids. Mouth-breather. Teeth: Good. Cervical glands: Enlarged; hard; movable; not tender; at angles jaw and posterior triangles.	99.6
J. M. 29195. Male. Med. No. 28435.	W	27	Tailor.	Frequent attacks tonsillitis for many years past. Had a severe attack 7 weeks ago; has never entirely recovered. Two weeks ago had headache, epistaxis, anorexia, vomiting and epigastric pain. Practically all joints involved, and a purpuric eruption on legs. This is first attack.	None.	Tonsils: Much hypertrophied; adherent to pillars. Nose: Approximately normal. Sinuses: Not infected. Ears: Normal. Nasopharynx: Chronically infected adenoids. Teeth: Pyorrhea; some carious. Cervical glands: Enlarged at angles jaw; slightly enlarged in both posterior triangles.	98.6
L. C. 29800. Female.	W	23	Seamstress.	Attacks of tonsillitis associated with rheumatism every winter since 8 years of age. Dyspnoea on exertion for many years. Heart flutters at times. Swelling of ankles on standing. Six weeks ago acute tonsillitis with chills, fever, and involvement of all joints, swollen, tender, red.	Mitral insufficiency.	Tonsils: Enlarged; adherent to pillars. Nose: Normal. Sinuses: Not infected. Ears: Normal. Nasopharynx: Small amount adenoids. Teeth: Many carious. Cervical glands: Enlarged at the angles of jaw; hard; movable; tender. Slightly enlarged in posterior triangles.	99
S. W. 29833. Female.	W	39	Housewife.	Tonsillitis at intervals since childhood. Acute rheumatic fever with involvement of practically all joints when 10 years of age; another attack when 29 years of age; a third attack 6 weeks ago. Joints red, hot, swollen and very painful; at present time are clearing up rapidly. Has lost 10 pounds in weight with this attack.	None.	Tonsils: Small; fibrous; adherent to pillars. Nose and sinuses: Normal. Nasopharynx: No adenoids. Ears: Normal. Teeth: Much dental work; X-ray: No infection. Cervical glands: Enlarged, tender at angles of jaw.	99.2

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
General glandular enlargement. Heart and lungs: Normal. Spine: Normal. Culture from tonsils after removal, staphylococci.)	Mar., 1914. Infected tonsils, adenoids. Cervical adenitis. Rheumatoid arthritis.	None.	June, 1915. Slight improvement in condition of joints according to patient. Back still stiff and painful. No new joints involved. Is able to work regularly.
General glandular enlargement. Heart and lungs: Normal. Spine: Normal. Marked muscular wasting around affected joints. B. C.: 4,000,000. H. C.: 8600. Hb.: 65%. Culture from tonsils after removal, staphylococci.) Gestive tract normal. Wassermann: Negative.	April, 1914. Infected tonsils. Rheumatoid arthritis.	None.	Aug., 1914. No improvement. More pain. New joints involved. Feb., 1916. Absolutely helpless for past year; gradually growing worse. Spine rigid; jaw ankylosed. Great pain.
General glandular enlargement. Heart: Crescendo murmur at left edge sternum replacing s' with each inspiration; not heard in expiration; not heard in axilla. Lungs: Fixation ribs; few râles over back at apex and base. No tbc. bacilli in sputum. Spine: Normal. U. tract: Normal.	May, 1914. Small, embedded tonsils. Enlarged gland at angle jaw on right. Rheumatoid arthritis.	Developed scarlet fever on 2d day after operation. Made normal recovery.	July, 1914. No improvement in joint condition. July, 1915. No improvement; some of joints worse; new joints involved. Neck and spine fixed and very painful. Cannot walk.
General glandular enlargement. Heart and lungs: Clear. Spine: Normal. Gynecological examination: Normal. B. C.: 3,900,000. H. C.: 5400. Hb.: 72%. M. M.: 53%. Tmph: 43%. Culture from tonsils after removal, staphylococci.)	May, 1914. Chronic tonsillitis. Cervical adenitis. Chronic infection nasopharynx. Secondary anæmia. Rheumatoid arthritis.	Bleeding from right tonsil due to slipping of catgut ligature. Vessel picked up with clamp and ligated with silver clip.	June, 1915. No improvement in joint condition. Spent several months in Hot Springs, Ark., without benefit. Is now bedridden. Reports that glands in neck are still enlarged and at times tender.
General glandular enlargement. Heart: Normal. Lungs: Slight impairment right apex and lower back. No tbc. bacilli found. Spine: Trace albumin, otherwise normal. B. C.: 7900. Hb. count normal.	July, 1914. Small infected tonsils. History frequent tonsillitis. Infected adenoids. Rheumatoid arthritis. (Extraction infected teeth; treatment pyorrhea.)	None.	June, 1915. No improvement. Has lost weight and strength. Contractures arms and legs. Bed ridden. Report throat normal.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
General glandular enlargement. The joints in both hands, left elbow, both knees, left hip were involved in last attack. Still slight redness, tenderness, swelling and pain on motion. B. C.: 8100. Hb.: 83%. Spine: Normal.	Dec., 1911. Repeated attacks tonsillitis. Rheumatic fever. Chorea.	None.	Jan., 1913. Following coryza had pain in right ankle and knee. Temperature 101° F. Was kept in bed for 4 weeks. No chorea. Oct., 1913. Has been well since last attack in Jan., 1913. All joints are normal at present. No chorea. Heart as before. Dec., 1913. In good shape. Throat looks normal; breathes normally through nose. Feb., 1914. In good shape. Heart condition the same; pulse strong and regular. No return of chorea. X-ray shows heart enlarged. Nov., 1914. In good shape. Has had no joint symptoms since Jan., 1913. Feb., 1915. Had another attack of acute rheumatic fever with multiple arthritis. Return of chorea. July, 1915. Seems perfectly free of all joint symptoms. Heart the same; compensation good. Temperature normal. No recurrence chorea.
General glandular enlargement. Spine: Slight trace albumin, otherwise negative. Erythematous eruption over both lower legs. Heart: Systolic murmur; not transmitted. Lungs: Normal. Multiple arthritis. B. C.: 12,800. Hb.: 85%.	Feb., 1912. Repeated attacks tonsillitis. Purpura rheumatica (Schönlein's disease). (Referred to dentist.)	None.	Aug., 1915 (over 3 years after operation). Has been working regularly since operation. No attacks of sore throat, rheumatism, or purpura. Joints all normal. No headaches. Remembers having had coryza on three occasions since operation. Glands are not palpable in anterior or posterior triangles, or in axillæ. Teeth in good condition. Throat and nasopharynx look normal with exception of chronic pharyngitis (smokes constantly). Heart: Normal. Pulse 72, regular. Liver and spleen not palpable. Urine: Normal.
General glandular enlargement. Thyroid: Enlarged; soft. Pulse rapid; regular. Lungs: Clear. Spine: Normal. Multiple arthritis. B. C.: 15,200. Hb.: 74%. Good culture: Negative.	May, 1912. Repeated attacks tonsillitis. Hyperthyroidism. Rheumatic fever. Multiple arthritis. Mitral insufficiency. (Extraction carious teeth.)	None.	June, 1915 (3 years after discharge from hospital). Has been in perfect health. Gained in weight. No sore throats; no further trouble with joints. Has been working regularly. Heart lesion well compensated. No longer swelling of ankles on standing.
General glandular enlargement. Heart and lungs: Normal. Spine: Normal. B. C.: 4,600,000. H. C.: 8700. Hb.: 70%. Wassermann: Negative.	May, 1912. Chronic tonsillitis. Rheumatic fever.	None.	Jan., 1916. Joints normal since Aug., 1912. General health much improved. No sore throat; colds very infrequent. Cervical glands not palpable. Heart: Normal.

TABLE V.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR ACUTE RHEUMATIC FEVER

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination. Tonsils, Nose, Sinuses, Ears, Nasopharynx, Teeth, Cervical Glands.	Temp. (Mouth on Day Before Operation. ° F.
G. C. 29854. Female.	W	12	School.	History of four severe attacks of tonsillitis with fever and chills. With last attack had precordial pain; dyspnoea; swelling, redness and pain in all joints. Hips particularly painful. Temperature was 105° F.	Acute fibrinous pericarditis. Mitral insufficiency.	Tonsils: Much enlarged; especially on right. Nose: Normal. Sinuses: Not infected. Ears: Chronic otitis media; suppurative. Nasopharynx: Large mass adenoids; mouth-breather. Teeth: Carious. Cervical glands: Enlarged; particularly on right in anterior triangle.	98.5
C. J. 30811.	C	12	School.	Has had frequent attacks tonsillitis. In 1911 had acute rheumatic fever with precordial pain, and involvement of all joints. In Jan., 1912, had second attack with fever; swelling and tenderness of joints. Dyspnoea on exertion. For the past month has had almost constant sore throat; enlarged cervical glands; unable to walk or use arms without pain.	Mitral insufficiency.	Tonsils: Enlarged, particularly on right; adherent to pillars; crypts filled with debris. Nose: Normal aside from discharge due to adenoids. Sinuses: Clear (X-ray diag.). Ears: Drums intact; tenderness over mastoid. Nasopharynx: Large mass adenoids; mouth-breather. Cervical glands: Size of walnut at angle jaw on right; soft; tender; movable. Also enlarged in all other triangles.	98.6
E. C. 30828. Female.	C	7		History three or four attacks tonsillitis every year for past 3 years. In 1911 following tonsillitis had swelling of joints; pain on motion; was confined to bed for six weeks. History choreiform movements at intervals for past year.		Tonsils: Much hypertrophied; adherent. Nose: Normal aside from discharge due to adenoids. Sinuses: Seem normal. Ears: Chronic catarrhal otitis media; no discharge. Nasopharynx: Large mass adenoids; mouth-breather; adenoid facies. Cervical glands: Enlarged at angle of jaw on both sides, especially right; also in posterior triangles.	99.6
A. W. 31004. Male.	W	15	Office.	Frequent tonsillitis; for past year almost constant sore throat. In 1910 had acute rheumatic fever; all joints involved; in bed 2 months. In 1911 a second attack rheumatic fever with multiple arthritis. Joints all normal at present. No history chorea. Tonsils "clipped" when 6 years of age.	Mitral insufficiency.	Tonsils: Enlarged; adherent to pillars. Adenoids: Large mass; infected. Ears: Normal. Teeth: Good. Cervical glands: Enlarged at angles jaw both sides.	
J. O'N. 31774. Male.	W	16	Office boy.	Infrequent tonsillitis; arthritis came on 2 months after sore throat which lasted 4 days. Has had four attacks polyarthritis in past 3 years. Only one attack associated with cold or sore throat. No history chorea. Complains of frequent attacks of palpitation heart.	Mitral insufficiency. Mitral stenosis. Tachycardia.	Tonsils: Enlarged; adherent to pillars. Nose: Normal. Sinuses: Not infected. Ears: Normal. Nasopharynx: Small amount adenoids. Cervical glands: Measure 3 x 5 cm. at angle jaw on both sides. (Culture from tonsils after removal showed pure culture streptococcus pyogenes.) Teeth: Carious.	98.4
M. P. 32484. Female.	W	36	Housewife.	Complains pain and stiffness of spine, also in elbows, fingers, and knees. History acute rheumatic fever with endocarditis and polyarthritis when 10 years of age. Joints soon cleared up and were normal until second attack rheumatic fever 3 years ago. After this the joints never became entirely normal. History frequent tonsillitis.	Adherent pericardium. Aortic insufficiency. Mitral insufficiency.	Tonsils: Small; fibrous; densely adherent to pillars. Nose: Normal. Sinuses: Clear. Ears: Normal. Nasopharynx: Small amount adenoids. Teeth: Carious lower molar on right. Cervical glands: Enlarged; hard; freely movable at angle jaw on each side. Slightly enlarged in both posterior triangles.	99
M. W. 33234. Female.	W	7		Frequent attacks tonsillitis with high fever, headaches and vomiting. Acute rheumatic fever 8 months ago. Joints never entirely returned to normal. No chorea. Is mouth-breather.	Mitral insufficiency.	Tonsils: Small; embedded; adherent. Teeth: Fairly good. Ears: Not infected. Nose: Normal, aside from discharge due to adenoids. Nasopharynx: Large mass adenoids; mouth-breather. Cervical glands: Enlarged at angles jaw. (Microscopical examination tonsils and adenoids after removal shows no tbc. lesion.)	99.2
S. C. 33586. Female.	W	12	School.	History of several attacks of rheumatic fever, last attack in Nov., 1913; at this time practically all joints were involved. The spine, both wrists and one hip have never entirely returned to normal. Has frequent headaches (due to eyes). Frequent sore throat; each attack makes affected joints worse.	None.	Tonsils: Much enlarged. Nose: Normal. Ears: Normal. Sinuses: All clear. Nasopharynx: Fairly large amount adenoid. Teeth: Good. Cervical glands: Much enlarged at angle jaw on both sides; also in both posterior triangles. (Culture for tonsils after removal: Streptococcus hæmolyticus.)	99.2
S. M. 34302. Male.	W	14	School.	In Feb., 1913, attack acute rheumatic fever with polyarthritis; joints entirely cleared up. In Jan., 1914, had second attack acute rheumatic fever with polyarthritis; precordial pain; was in bed for 3 months. No history tonsillitis.	Acute pericarditis. Adherent pericardium. Mitral insufficiency.	Tonsils: Very large; meet in mid-line; adherent to pillars. Nose: Hypert. inf. turb.; otherwise normal. Sinuses: Clear. Ears: Normal. Nasopharynx: Small mass adenoids; had been previously removed. Cervical glands: Enlarged, tender in anterior and posterior triangles.	99
W. S. 34780. Male.	W	8		History occasional sore throats for past 3 or 4 years; about 2 months ago had tonsillitis followed in a few days by chills; high fever; swelling, redness, pain knees, ankles, hands, wrists, elbows. No history chorea.	None.	Teeth: Many carious. Tonsils: Greatly enlarged. Nose: Normal except discharge from adenoids. Sinuses: Not infected. Ears: Normal. Nasopharynx: Large mass adenoids; mouth-breather. Teeth: Carious. Cervical glands: Enlarged at angle jaw on both sides.	98.4

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
General glandular enlargement. Throat: Clear. Lungs: Clear. T. B. C.: 3,800,000. R. B. C.: 16,200. Hb.: 60%.	May, 1912. Repeated attacks tonsillitis. Pericarditis. Mitral insufficiency. Rheumatic fever. (Extraction carious teeth.)	None.	July, 1915. Had recurrence of joint symptoms July, 1912 (2 months after leaving hospital). In Dec., 1913, had severe attack arthritis involving ankles, knees, wrists; was confined to bed for several months. Still has some stiffness and impairment of motion in right wrist and ankle. Has had no sore throats since operation, but above attacks were associated with coryza, headache, vomiting and fever. Is a healthy, well-nourished child. Teeth: Carious. Ears: No discharge; drum intact; hearing normal. Heart: Enlarged; systolic murmur heard in axilla and back; no pericardial rub.
General glandular enlargement. Lungs: Slight impairment left apex; no rales. Throat: Normal. T. B. C.: 10,400. Hb.: 67%.	Oct., 1912. Frequent attacks tonsillitis. Mitral insufficiency. Rheumatic fever.	None.	May, 1913 (7 months after operation). Joints all normal. Has frequent colds; no sore throat. Difficulty in breathing through nose due to hypert. of both inf. turb. Nasopharynx and throat look normal. Glands of neck barely palpable. Has gained weight. June, 1915. On one or two occasions since last note has had some stiffness in joints for 2 or 3 days at a time. All joints normal now. Has worked regularly since Dec., 1912; has not lost a day on account of sickness. Glands in anterior triangles are not palpable. Teeth in good condition. Nose: The hypert. of the inf. turb. has disappeared; now looks normal. Heart: Not enlarged; P. M. I. 1 cm. inside m. line; sounds normal at apex and base.
General glandular enlargement. Lungs: Clear. Heart: Not enlarged; systolic murmur at apex, not well heard in axilla. Throat: Normal. Movements of both arms and legs.	Nov., 1912. Frequent attacks tonsillitis. Rheumatic fever. Endocarditis? Chorea.	None.	May, 1913. Has had no return of arthritis or chorea. Breathes normally through nose; has grown rapidly; appetite good. Glands in cervical triangles are still slightly enlarged. Heart sounds clear. Mar., 1914. No return of chorea or arthritis. No evidence of any heart lesion. Ears: Hearing normal; drums intact. Teeth: Good. Aug., 1915. General health excellent. No return of arthritis or chorea. Heart normal.
No general glandular enlargement. Heart: 9½ cm. to left from mid-line; not enlarged to right. Systolic murmur at apex, axilla and back. Lungs: Regular; no arteriosclerosis. Lungs: Clear on perc. and ausc. Liver and spleen: Not palpable. T. B. C.: 6300. Hb.: 84%.	Nov., 1912. Chronic tonsillitis. Infected adenoids. Cervical adenitis. History two attacks rheumatic fever.	None.	Mar., 1914. Has been perfectly well since operation. Throat and nasopharynx look normal. No recurrence of arthritis. Gained 35 pounds in weight. Joints normal. Sept., 1915. Perfectly well; works regularly. Cervical glands not palpable. No symptoms of heart lesion. Joints normal. Heart: Apex in 5th s. Dullness 11 cm. to left of mid-line; 3½ cm. to right in 4th s. A soft systolic murmur at apex not transmitted to axilla. Sounds clear at base. Perfect compensation.
General glandular enlargement. Lungs: Clear. Heart: Not enlarged; systolic murmur at apex transmitted to axilla and back; also faint murmur at base. Liver: Not enlarged. Spleen: Palpable. Lungs: Clear on posterior and anterior. T. B. C.: 9600. Culture from tonsils after removal; (staphylococcus.)	Mar., 1913. Three attacks acute rheumatic fever. Mitral insufficiency and stenosis. Renal lesion. (Extraction carious teeth.)	Elevation of temperature to 101° F. Right wrist and shoulder became hot, swollen, painful; was apparently normal before operation. Rapidly cleared up.	May, 1913 (2 months after tonsillectomy). Joints all seem normal. Appetite good. Cervical glands still enlarged. Heart: 11 cm. left; 4 cm. to right; murmurs as before.
No general glandular enlargement. Lungs: Clear. T. B. C.: 7000. Hb.: 90%.	July, 1913. Attacks tonsillitis. Rheumatic fever. Heart lesions. Arthritis. (Extraction carious teeth.)	None.	Mar., 1914. Glands at angle jaws not palpable. Teeth in good shape. Throat, nose and nasopharynx normal. Has gained weight. The axillary and epitrochlear glands are much smaller. Urine: Normal. Dec., 1915. Is a strong, healthy looking man; has had no illness of any kind for 2 years. Works regularly. Urine: Normal. Heart: Much smaller; well compensated. Has no more paroxysmal tachycardia. The anterior cervical glands are not palpable on left; barely felt on right. Throat looks normal aside from hypertrophic pharyngitis.
General glandular enlargement. Heart: Slightly enlarged. Systolic murmur at apex transmitted to axilla and back; also faint murmur at base. Liver: Not enlarged. Spleen: Palpable. Lungs: Clear on posterior and anterior. T. B. C.: 9600. Culture from tonsils after removal; (staphylococcus.)	Nov., 1913. Chronic tonsillitis. Rheumatic fever. Heart lesion. Tbc. synovitis.	None.	June, 1915. There has been no improvement in the arthritis of the lower spine; the elbows, fingers and knees are improved but not normal. Still painful and very stiff early in mornings, and during rainy weather. Cervical glands not palpable. Heart lesion well compensated. There has been no increase in the joint symptoms or involvement of other joints.
General glandular enlargement. Lungs: Clear. Heart: Normal. Throat: Normal.	Jan., 1914. Frequent tonsillitis. Rheumatic fever. Arthritis.	None.	Mar., 1914. Joints all normal with exception left ankle. No colds or sore throat since operation. April, 1914. Re-admitted to hospital and operated on for tbc. synovitis left ankle. April, 1915. Ankle well; no other joints involved. No evidence Tbc. elsewhere. General health better than ever before. Aug., 1915. No return arthritis. Cervical glands barely palpable. Spleen not felt. Nose, throat, ears normal. Teeth carious. Heart: Not enlarged to right or left. Systolic murmur, maximum at apex, heard in axilla and back. No diastolic murmur. No shock or thrill. Well compensated lesion.
General glandular enlargement. Epitrochlears large. Axillary glands tender. Wassermann: Negative. Lungs: Slight dullness left lower back; just recovered from pneumonia. T. B. C.: 3,800,000. R. B. C.: 13,400. Hb.: 65%.	Apr., 1914. Rheumatic fever. Heart lesions. Arthritis. (No history tonsillitis.) (Referred to dentist.)	None.	July, 1915 (18 months after tonsillectomy). Still has pain at times in back, but no limitation of motion at present. The wrists and hip have cleared up; now appear normal in every way. The cervical glands are still enlarged in both anterior and posterior triangles. There is one carious tooth (referred to dental department).
General glandular enlargement. Lungs: Clear. Heart: Normal. Throat: Normal. Urine: Albumin and R. b. c. No casts.	June, 1914. Attacks tonsillitis. Rheumatic fever. Renal lesion.	None.	Jan., 1916 (over 1½ years after tonsillectomy). Joints have all cleared up; no stiffness or pain for over a year. Glands at angle jaw on each side measure about 2 cm. in diameter; other smaller glands in anterior triangles; none palpable in posterior triangles. Teeth: Many filled. Nose: Hypert. inf. turb. left. "General health better than ever before." Heart: P. M. I. 4 s., 2½ cm. inside m. line. Not enlarged to right. No palpable thrill. Mitral insufficiency as before. No friction rub heard. Pulse regular and strong; 80 to minute.
			Aug., 1915 (over 1 year after tonsillectomy). Joints normal; has had no recurrence of joint symptoms. Had acute otitis media last winter; ears are normal at present time. Glands in anterior triangles not palpable; measure about ½ cm. in diameter in posterior triangles. Teeth in good condition. Nose, throat, and nasopharynx look normal. Axillary and epitrochlear glands still palpably enlarged. Urine: Normal in every way; no trace of albumin.

TABLE V.—ARTHRITIS GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR ACUTE RHEUMATIC FEVER

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examinations. Tonsils, Nose, Sinuses, Ears, Nasopharynx, Teeth, Cervical Glands.	Temp. (Mouth) on Day Before Operation. ° F.
S. P. 34838. Male.	W	22	Student.	Trouble with nose and throat all his life. Frequent and severe "winter colds," and attacks tonsillitis. Has had three attacks rheumatic fever in past 8 years. Last attack 1 month ago was associated with tonsillitis. No chorea.	Mitral insufficiency.	Tonsils: Enlarged; very adherent to pillars. Nasopharynx: Infected adenoids. Ears: Normal. Nose: Hypert. inf. turb.; sinuses clear. Teeth: Good. Cervical glands: Slightly enlarged angle jaws both sides; just palpable in posterior triangles.	99.6
H. F. 34859. Male.	W	25	Student.	Frequent tonsillitis during past 2 years. Last attack of tonsillitis was followed 4 days later by acute rheumatic fever; pericarditis with effusion; and myocarditis. All joints were affected, but left knee and hip cleared up more slowly than others.	Pericarditis with effusion. Myocardial insufficiency.	Tonsils: Enlarged; densely adherent to pillars. Nose: Hypert. inf. turb.; no sinus infection. Ears: Normal. Nasopharynx: Small amount adenoids; discharge from posterior nares. Teeth: Good. Cervical glands: Enlarged at angles jaw and in posterior triangles.	98.4
E. McC. 35084. Female.	W	7		History frequent tonsillitis since early childhood. Is said to have had "muscular rheumatism" 3 years ago. Has had two attacks of rheumatic fever within the past 1½ years. Both associated with tonsillitis. All joints of legs involved. Has fever and sore throat almost constantly for past month. Joints are stiff and painful on motion.	Mitral insufficiency.	Tonsils: Not enlarged; adherent to pillars. Nose: Normal. Sinuses: Not infected. Teeth: Carious. Ears: Drums intact; hearing good. Nasopharynx: Moderately enlarged. Cervical glands: Enlarged in anterior and posterior triangle on both sides.	100
B. T. 35494. Female.	W	13	School.	Frequent tonsillitis. Mouth-breather. Frequent epistaxis. Acute rheumatic fever with heart lesion and multiple arthritis 6 years ago. Has been dyspnoic since on slight exertion. Joints still stiff and at times very painful. No chorea.	Mitral insufficiency.	Tonsils: Enlarged; especially on left; adherent to pillars. Teeth: Many carious; alveolar abscess. Ears: Chronic catarrhal otitis media. Nose: Normal aside from discharge due to adenoids. Nasopharynx: Chronically infected adenoids. Mouth-breather. Cervical glands: Enlarged in all triangles.	98
E. H. 35753. Female.	W	12	School.	History frequent tonsillitis, and discharge from both ears 1 year ago. Has had one attack of polyarthritis involving the large and small joints, with fever and sore throat. Some pain over heart. Joints normal at present. Frequent headaches.	Mitral insufficiency.	Tonsils: Much enlarged. Nose: Deflected septum to right; discharge on right. Teeth: Good. Nasopharynx: Large mass adenoids; mouth-breather; adenoid facies. Ears: Purulent discharge both sides. Cervical glands: Enlarged at angle jaw both sides; smaller in posterior triangles.	98.5
H. C. 36124. Male.	W	25	Farmer.	Following an attack of tonsillitis 5 years ago had high fever and swelling, redness, tenderness of joints of legs and arms. Has had frequent recurrence of these attacks. At present the back is stiff and painful. Headaches.	Mitral insufficiency.	Tonsils: Both small, fibrous, densely adherent to pillars. Nose: Obstruction due to deflected septum; hypert. of inf. turb. and mid. turb. on left. X-ray: Shows clouding left frontal sinus. Teeth: Good. Ears: Chronic catarrhal otitis media; tinnitus. Nasopharynx: Discharge from left side nose; chronic pharyngitis. Cervical glands: Enlarged on both sides at angle jaw. Chain of enlarged glands in both posterior triangles.	98.4
K. G. 36180. Female.	W	10	School.	No history of tonsillitis. Complains pain in chest; skin rash (urticaria); pain, swelling, redness of joints; headaches. First attack arthritis 1 year ago; last attack 1 month ago. Joints still painful; has been in bed for 3 weeks. Frequent colds and cough; dyspnoea on exertion.	Aortic insufficiency. Mitral insufficiency.	Tonsils: Much enlarged; adherent to pillars. Nose: Right inf. turb. enlarged; sinuses clear. Teeth: Good. Ears: Normal. Nasopharynx: Large mass adenoids; mouth-breather. Cervical glands: Enlarged in both anterior and posterior triangles.	99.6
H. C. 36205. Female.	W	18	Clerk.	Has had two admissions to this hospital for acute rheumatic fever. First attack in Feb., 1914; associated with streptococcic tonsillitis; endocarditis; multiple arthritis. Joints cleared up. Second attack July, 1914. Came on about 1 month after a severe tonsillitis. Knees chiefly affected. Since this attack joints stiff and painful; walks with difficulty, using a cane. No history chorea.	Mitral insufficiency.	Tonsils: Enlarged; adherent; infected. Adenoids: Small; chronically infected; discharge. Ears: Not infected. Nose: No sinus infection. Teeth: Gingivitis; caries. Cervical glands: Enlarged at angles jaw; tender. Just palpable in posterior triangles.	98.6
S. M. 36430. Male.	W	14		Frequent tonsillitis. Has had five or six attacks acute polyarthritis during past 3 years. Frequent frontal headache; chronic supp. otitis media; swelling glands left side neck. Dyspnoea on exertion for past year; also edema feet and ankles 1 year at frequent intervals.	Mitral insufficiency.	Tonsils: Enlarged; adherent to pillars. Adenoids: Enlarged. Teeth: Carious. Sinuses: Not infected. Ears: Chronic supp. otitis media. Cervical glands: Size walnut angle jaw left; enlarged in other triangles.	
D. S. 37036. Female.	W	9		Frequent tonsillitis. Has had three attacks of multiple arthritis. Chorea after last attack. Complains pain over heart. Dyspnoea on exertion.	Mitral insufficiency.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Carious. Sinuses: Not infected. Cervical glands: Enlarged in anterior and posterior triangle.	99.5
H. W. 37212. Male.	W	13	Factory.	Occasional sore throat. Has had one attack of multiple arthritis 1 month ago involving hips, knees, ankles. Joints swollen, hot, red, very painful. No history chorea.	Mitral insufficiency.	Tonsils: Enlarged; adherent to pillars. Adenoids: Very large. Teeth: Good. Sinuses: Not infected. Cervical glands: Enlarged in anterior and posterior triangles.	99

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Slight glandular enlargement. Heart: Slightly enlarged; definite mitral lesion. Lungs: Clear on perc. and ausc. Urine: Normal. R. B. C.: 4,900,000. W. B. C.: 13,600. Hb.: 95%.	June, 1914. Chronic tonsillitis. Rheumatic fever. Heart lesion. (Nasal operation also.)	None.	Oct., 1915. No recurrence of joint symptoms. No colds or sore throat during past winter. Heart: Well compensated lesion. Nose and throat look normal.
General glandular enlargement. Lungs: Normal. Urine: Trace albumin; no casts; no blood. R. B. C.: 5,600,000. W. B. C.: 4750. Hb.: 95%.	June, 1914. Frequent tonsillitis. Rheumatic fever. Pericarditis. Myocarditis.	None.	July, 1914. Three weeks after tonsillectomy had relapse with return of joint symptoms, and alarming myocardial insufficiency; slowly recovered. Feb., 1916. General health excellent since Aug., 1914. Has had no sore throat, nor any return of joint symptoms. The cervical glands are still enlarged on both sides. Aug., 1916. Joints all normal. General health excellent.
Culture from tonsils after removal; streptococcus hæmolyticus. General glandular enlargement. Axillary glands tender. Lungs: Clear on perc. and ausc. Urine: Normal.	Aug., 1914. Frequent tonsillitis. Rheumatic fever. Heart lesion.	None.	April, 1915. General health excellent; growing rapidly. Joints all normal. No dyspnoea on running, as before. Nasopharynx and throat normal. Heart: Loud systolic murmur heard in axilla and over back. Aug., 1915. Glands in anterior triangles not palpable; just felt in posterior triangles. Joints normal. Liver and spleen not palpable. Heart: The systolic murmur is soft, blowing in character; heard loudest at P. M. I.; transmitted to axilla and back. Cardiac dullness extends 8½ cm. to left in 5 i. s.; to sternal border in 4 i. s. Pulse: Regular.
Slight general glandular enlargement. Heart: Enlarged to left. Systolic murmur at apex, axilla and back. Lungs: Clear on perc. and ausc. Urine: Normal.	Oct., 1914. Chronic tonsillitis. Rheumatic fever. Heart lesion. Arthritis. (Extraction carious teeth.)	None.	Aug., 1915. No recurrence arthritis. Joints all normal at present. No chorea. No sore throat or cold since operation. No shortness of breath; can take exercise like other children. Goes to school regularly for the first time in her life. Cervical glands not palpable. Teeth, nose, throat, ears all look normal.
Glands, axillæ, groins, epitrochlears enlarged. Lungs: Normal. Urine: Normal. Is a pale, slender, ææmic looking child.	Nov., 1914. Frequent tonsillitis. Rheumatic fever. Chronic supp. otitis media double. Mouth-breather. Heart lesion.	None.	April, 1915. Has gained weight. General health good. No sore throat and no joint symptoms since operation. Has no dyspnoea on exertion. Glands neck just palpable. Ears: No discharge; drums intact; hearing within normal limits. Teeth: Carious (referred to dentist). Heart: As before. Aug., 1915. Discharge in nasopharynx due to infection right antrum (X-ray: Clouding right antrum). Teeth still in bad shape. Glands: Chain in each posterior triangle about ½ cm. in diameter; smaller in anterior triangles. Chronic hyperplastic pharyngitis. (Irrigation antrum.) Heart: P. M. I. in 4 s. 5.3 cm. to left mid-sternal line; right heart 1.5 cm. to right sternum. P ² accentuated. No thrill. Blowing systolic murmur, maximum at apex, transmitted to axilla and back.
Slight general glandular enlargement. Lungs: Clear on perc. and ausc. Urine: Albumin; no casts; no R. B. C. Bradycardia: Pulse 50 to minute, but regular and strong.	Jan., 1915. Frequent tonsillitis. Rheumatic fever. Arthritis. Heart lesion. (Nasal operation also.)	None.	Sept., 1915. No improvement in condition of back; other joints still stiff, and at times painful. Still has tinnitus. (Advised operation on sinuses.)
General glandular enlargement. Lungs: Few râles heard over both lungs; slight impairment at apices. Pirquet: Positive. (No histological evidence of Tbc. in tonsils or adenoids.) Urticarial rash fading. Blood culture negative.	Jan., 1915. Urticaria. Rheumatic fever. Arthritis. Heart lesions.	None.	Oct., 1915. Glands in neck still slightly enlarged on both sides. Hypertrophic pharyngitis, otherwise throat and nasopharynx normal. Sinuses: Clear. General condition good.
Slight general glandular enlargement. Heart: Enlarged to left; definite mitral lesion. Lungs: Clear on perc. and ausc. Urine: Albumin; no casts; no blood. W. B. C.: 10,700. Hb.: 79%.	Jan., 1915. Chronic tonsillitis. Rheumatic fever. Chronic arthritis. (Referred to dentist.)	None.	April, 1915. Heart: 9 cm. to left in 5 s.; 2 cm. right in 4 s. Pulse 84. Blowing diastolic murmur at aortic area after exertion. No thrill. June, 1916. General condition good. No glandular enlargement. Lungs clear on posterior and anterior. Heart: 8 cm. to left in 5 s.; 2 cm. to right in 4 s. Sounds clear at apex.
General glandular enlargement. Lungs: Clear on perc. and ausc. Urine: Albumin and casts. Phthalein: 58% for 1st h.; 10% for 2d h. R. B. C.: 4,200,000. W. B. C.: 11,600. Hb.: 72%.	Feb., 1915. Chronic tonsillitis. Rheumatic fever. Heart lesion. Otitis media. (Extraction carious teeth.)	Acute flare-up of arthritis involving right shoulder, elbow, wrists and fingers. Gradually subsided.	June, 1915. Joint condition has gradually improved; for past 3 months walks normally; no pain; occasional stiffness. Cervical glands not palpable on either side in anterior triangles. Throat normal with exception of hypertrophic pharyngitis. Nasopharynx: Normal. Nose normal. Heart: Enlarged; 11½ cm. to left mid-line; 4 cm. right. Blowing systolic murmur at apex, over sternum and in axilla. P ² accentuated. Liver not enlarged. Pulse regular.
Differential blood count; normal. Lungs: Clear on perc. and ausc. Heart: Enlarged; blowing systolic murmur apex, axilla and back. Urine: Normal.	May, 1915. Chronic tonsillitis. Heart lesion. Rheumatic fever.	None.	July, 1915. Recurrence acute arthritis 1 month ago; not so severe as usual, was in bed for a week. No headaches since tonsillectomy. Ears: Drums intact; hearing good. Teeth: Good. Cervical gland on left is barely palpable; measures about 1 cm. in diameter. Heart: P. M. I. in 5th s. 7½ cm. left of mid-line; right border 2 cm. right mid-line. Systolic murmur heard all over back. No thrill. Pulse: Regular, 96 to minute. Liver: Slightly enlarged. Spleen: Not palpable. No general glandular enlargement.
Lungs: Clear. Heart: Enlarged; systolic murmur apex, heard in axilla. Urine: Normal. R. B. C.: 4,700,000. W. B. C.: 5600. Hb.: 77%.	June, 1915. Chronic tonsillitis. Heart lesion. Rheumatic fever.	None.	May, 1916. Joints normal. No recurrence rheumatic fever or chorea since operation. No pain over heart. No dyspnoea. General condition excellent. Heart: Left border 7 cm. left mid-line; right border 1 cm. right of sternal margin. Systolic murmur as before.
			Nov., 1915. Joints normal. No recurrence arthritis since operation. Works regularly. Cervical glands not palpable. Throat: Normal. Heart: Murmur as before. Pulse 90, regular. Oct., 1916. No recurrence rheumatic fever or arthritis. Works regularly.

TABLE VI.—REMOVAL OF TONSILS AND ADENOIDS FOR SYDENHAM'S CHOREA

I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mout on Day Before Operation. ° F.
A. L. 30988. Female.	W	5		Frequent sore throats for past 3 years. Onset chorea 2 months ago; never arthritis. Twitching in both arms and face; less marked legs. Speech thick.	Mitral insufficiency.	Tonsils: Much enlarged; crypts filled with yellowish plugs of debris. Teeth: Many carious. Nose: Negative aside from discharge due to adenoids. Ears: Normal. Nasopharynx: Large mass adenoids. Cervical glands; all enlarged.	98.6
S. A. 35735. Female.	W	5		No history sore throat; colds infrequent. Onset 2 weeks ago with multiple arthritis affecting hips, both ankles and left elbow. Irregular jerking movements in hands, arms and legs.	None.	Tonsils: Much enlarged. Nasopharynx: Large adenoids; mouth-breather. Discharge from nose. Teeth: Good. Ears: Not infected. Cervical glands: Enlarged particularly at angles jaw; also in posterior triangles.	98.8
M. K. 37441. Female.	W	4		No history of sore throat; was in Robert Garrett Hospital for 2 months with acute chorea. No arthritis. No heart lesion. Both hands, arms and legs involved; jerky, irregular movements. Eczema; no history asthma.	None.	Tonsils: Not particularly enlarged. Nasopharynx: Adenoids; mouth-breather. Teeth: Good. Ears: Normal. Nose: Slight discharge due to adenoids. Cervical glands: Enlarged at angles jaw and in posterior triangles. Has eczema behind left ear.	99
B. M. 35464. Female.	W	3		Has had tonsillitis once or twice. First attack tonsillitis in 1910.	None.	Tonsils: Enlarged. Adenoids: Very large mass. Teeth: Many carious. Cervical glands: Visible on inspection at angles jaw.	99

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

J. R. 30827. Male.	C	7		History frequent attacks tonsillitis. First attack chorea in 1910. Was treated in dispensary of the Johns Hopkins Hospital.	None.	Tonsils: Much enlarged. Nasopharynx: Large mass adenoids. Cervical glands: Enlarged on both sides in anterior triangles.	99.5
R. B. 30417. Male.	W	9		Very indefinite history of tonsillitis. Is mouth-breather. Has frequent "colds." Is just recovering from fourth attack of chorea. Has marked difficulty in articulating. History of weakness one leg and arm.	None.	Tonsils: Small; atrophic; adherent to pillars. Adenoids: Large; discharge from nasopharynx. Teeth: Good. Nose: Normal aside from discharge due to adenoids. Ears: Normal. Cervical glands: Slightly enlarged in anterior and posterior triangles.	98
E. C. 30828. Female.	W	7		Frequent tonsillitis; three or four attacks a year for past 2 years. Has had two attacks acute rheumatic fever; the last about 1 year ago. Joints all clear at present. Chorea, both arms and legs, at intervals for 2 years. Jerking at present.	Mitral insufficiency.	Tonsils: Very large; especially right; chronically infected. Nasopharynx: Adenoids enlarged; infected; adenoid facies; mouth-breather. Teeth: Carious. Ears: Not infected; hearing good. Cervical glands: Enlarged at angles jaw, particularly on right.	99.6
H. G. 30953. Male.	W	8	School.	Frequent "colds"; occasional sore throat; mouth-breather. Tonsillitis about 2 months ago followed by irregular jerking of muscles of face, and both upper arms. No history similar trouble previous to this attack. Has headaches, probably due to eyes. No arthritis.	None.	Tonsils: Much enlarged. Nasopharynx: Adenoids much enlarged; mouth-breather; adenoid facies. Ears: Normal. Nose: Normal aside from discharge due to adenoids. Teeth: Carious. Cervical glands: Enlarged at angles jaw; smaller in posterior triangles.	98.6
R. A. 29279. Male.	W	8	School.	History occasional sore throat and coryza. Acute rheumatic fever 2 years ago. Onset gradual 1 month ago, with jerking of arms, legs, and face. Pains in all of larger joints of arms and legs; some swelling of affected joints. Drags left leg on walking for 3 weeks. Speech very much impaired.	Mitral insufficiency.	Tonsils: Very large; adherent to pillars. Nasopharynx: Large mass adenoids; mouth-breather. Teeth: In good condition. Nose: Normal aside from discharge due to adenoids. Ears: Not infected. Cervical glands: Enlarged in all triangles.	98.6
M. A. 33218. Female.	W	9	School.	Tonsillitis every winter since 2 years of age; frequent "colds." Has had three attacks of chorea; no symptoms at present. Acute rheumatic fever 8 months ago with heart lesion resulting. Joints normal at present.	Mitral insufficiency.	Tonsils: Very large; adherent to pillars; crypts filled with yellowish debris. Teeth: Carious. Nose: Deflected septum to left; discharge on both sides. Ears: Chronic catarrhal otitis media. Nasopharynx: Large, infected adenoids; mouth-breather. Cervical glands: Much enlarged both anterior triangles.	99
I. M. 33489. Female.	W	10	School.	Tonsillitis 6 weeks ago followed by chorea; still has choreiform movements of arms, legs and face. Also pains and stiffness in joints.	Mitral insufficiency.	Tonsils: Small; fibrous; adherent to pillars. Teeth: Good condition. Nose: Normal. Ears: Drums retracted. Nasopharynx: Adenoids have been removed. Cervical glands: Slightly enlarged at angles jaw.	
B. G. 34743. Female.	W	10	School.	Frequent attacks tonsillitis. No history arthritis. Choreiform movements of arms and legs at present. No history heart trouble. Is very nervous and irritable.	June, 1914, none. Feb., 1915, mitral insufficiency.	Tonsils: Not enlarged; densely adherent to pillars. Teeth: Carious. Ears: Normal. Nose: Good breathing space. Nasopharynx: Large mass adenoids; mouth-breather. Cervical glands: Enlarged at angles jaw.	99

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative. Complications.	Subsequent Examination.
Marked general glandular enlargement. Heart: Enlarged; systolic murmur heard in axilla and back. Lungs: Clear. Spleen: Enlarged. Retrosternal dullness; X-ray diagnosis: Persistent thymus. Urine: Trace albumin; no casts found. t. B. C.: 4,900,000. W. B. C.: 14,400. Hb.: 80%.	Nov., 1912. Chorea. History sore throat. Mouth-breather. Mitral insufficiency.	Elevation of temperature to 101° F., and pulse 145 for 2 days; rapidly returned to normal. (Blood culture negative.)	May, 1913. No evidence of chorea since operation. Mother says child is much less nervous. Throat, nasopharynx and nose look normal. Glands of neck, axilla, groins much smaller. Temperature normal.
General glandular enlargement. Heart: Not enlarged; systolic murmur at apex and left sternal border, not transmitted. Lungs: Clear. Urine: Normal. t. B. C.: 5,500,000. W. B. C.: 21,600. Hb.: 92%.	Nov., 1914. Enlarged tonsils. Mouth-breather. Cervical adenitis. Chorea. Infectious arthritis. Purpura.	None.	Jan., 1914. Admitted to hospital with acute chorea; arthritis; elevated temperature; dilatation of heart. Succumbed a few day later. No autopsy.
Purpura on lower legs. No general glandular enlargement. Heart: Normal. Lungs: Normal. Urine: Normal.	July, 1915. Chorea. Cervical adenitis. Mouth-breather. (Referred to skin department for eczema.)	None.	April, 1915. Joints normal for past 4 or 5 months. No return of chorea which completely disappeared soon after operation. The cervical glands are just palpable; a little larger on right side. Heart normal. Throat looks normal. Still discharge from nose particularly left.
Mouth-breather. Deformity of chest due to adenoids. Heart and lungs: Clear. Urine: Clear.	Oct., 1914. Chronic tonsillitis. Cervical adenitis. Chorea.	None.	July, 1915. Returns on account lump at angle jaw on left; noticed for 2 months. Is slightly tender, firm, movable; measures 2 x 3 cm. Glands in posterior triangles and on right are barely palpable. Pirquet test: Negative. Still some nasal discharge. Joints normal. No return of chorea. Appetite excellent; has gained weight. Temperature normal. Heart and lungs normal. Urine normal.
			Nov., 1915. No return of any of the symptoms of chorea. Glands neck much smaller. Throat and nasopharynx look normal with exception of hypertrophic pharyngitis.
			Oct., 1916. No recurrence of chorea. Mother states child has had no symptoms of nervousness since operation. General health good. Is gaining weight.
			Nov., 1915. No recurrence chorea. General health good. Nose, throat and ears look normal. Cervical glands still palpably enlarged; size lima bean on right; smaller on left at angle jaw.
			Nov., 1916. No recurrence chorea. "Perfectly well since operation."

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

Heart and lungs: Clear. Urine: Normal.	Nov., 1912. Chronic tonsillitis. Cervical adenitis. Chorea.	None.	Nov., 1916. Has occasional symptoms of chorea at intervals since operation, but mother says "nervousness" is much improved. Does not articulate clearly. General health good. Teeth: Carious; alveolar abscess. Cervical glands just palpable. Nose, throat and ears look normal aside from teeth.
Light general glandular enlargement. Heart: Not enlarged. A murmur (systolic) heard at apex. Not transmitted. Lungs: Normal. Urine: Normal. t. B. C.: 8200. Hb.: 80%.	Aug., 1912. Repeated attacks chorea. Small, fibrous tonsils. Mouth-breather.	None.	Mar., 1914. Had another attack acute chorea; died in St. Agnes' Hospital. No autopsy.
General glandular enlargement. Heart: Slightly enlarged; loud, rough systolic murmur at apex; heard in axilla and over back. Lungs: Normal. Urine: Normal.	Nov., 1912. Frequent tonsillitis. Acute rheumatic fever. Chorea.	None.	May, 1913. No recurrence of joint symptoms or chorea. General health and appetite much improved. Nose, nasopharynx and throat look normal aside from hypertrophic pharyngitis. Glands neck barely palpable. Heart: Normal size; very faint systolic murmur.
General glandular enlargement. Heart: Normal. Lungs: Normal. Urine: Normal. t. B. C.: 9300. Hb.: 92%.	Nov., 1912. History tonsillitis. Mouth-breather. Chorea. (Referred to oculist.) (Extraction carious teeth.)	Bleeding from nasopharynx at intervals for a week. Very difficult to control with packing. Marked secondary anemia; Hb. from 92% to 40%.	Mar., 1914. In perfect health since tonsillectomy. Joints normal. No recurrence chorea. Glands neck not palpable; those in groin and axillæ just felt. Spleen not palpable. Heart: No evidence of any lesion; not enlarged; no murmur.
Marked general glandular enlargement. Axillary glands on left being 2 cm. in diameter. Heart: Enlarged to right and left; systolic murmur at apex heard in axilla and back. Also a proto-diastolic gallop at apex. Lungs: Clear on perc. and ausc. Urine: Clear. Erythema multiforme. t. B. C.: 5,400,000. W. B. C.: 5400. Hb.: 82%.	Feb., 1912. Chronic tonsillitis. History rheumatic fever. Chorea. Heart lesion.	None.	July, 1915. No recurrence of chorea. Is still having trouble with eyes. Is a well-grown, healthy looking boy. Heart normal. Glands: Barely palpable in neck, axillæ and groins. Hypertrophic pharyngitis, otherwise throat normal. Still carious teeth.
Marked general glandular enlargement. Heart: Enlarged to left; systolic murmur at apex; transmitted to axilla and back. Dyspnoea: On exertion. Lungs: Clear. Urine: Normal. t. B. C.: 5,000,000. W. B. C.: 12,400. Hb.: 70%.	Nov., 1913. Chronic tonsillitis. Cervical adenitis. Acute rheumatic fever. Chorea. Heart lesion. (Extraction carious teeth.)	None.	April, 1915 (over 3 years after operation). Has been in perfect health. No recurrence of chorea or arthritis. Cervical glands still slightly enlarged on left; not palpable on right in anterior triangle. Nose and throat look normal. Is now a well-nourished and well-developed boy. No subcutaneous nodules felt. Heart: Slightly enlarged, but no murmurs to be heard.
No general glandular enlargement. Heart: Enlarged; mitral insufficiency. Lungs: Clear on perc. and ausc. Urine: Normal. t. B. C.: 12,200. Hb.: 82%.	Dec., 1913. History tonsillitis. Chorea. Heart lesion.	None.	Feb., 1914. Admitted to hospital with recurrence chorea; chiefly in one hand. Heart as before. No return of arthritis. Teeth carious. Cervical glands enlarged. Spleen palpable.
No general glandular enlargement. Heart: 7 cm. to left mid-line; 1½ cm. to right mid-line. Systolic murmur; loudest at apex but heard along left sternal border; not transmitted. Lungs: Impaired percussion note left upper; no râles. Urine: Normal.	June, 1914. Chronic tonsillitis. Cervical adenitis. Chorea.	None.	Feb., 1915. Admitted with second recurrence chorea; mild attack. No joint symptoms. Chorea cleared up after six weeks in bed.
			Nov., 1915. Since discharge from hospital in Mar., 1915, general health has been excellent. No joint or chorea symptoms. Heart as before.
			Jan., 1914. No recurrence chorea. Very nervous. Still complains of joints.
			April, 1915. Vague pains in limbs and chest. Examination negative aside from old heart lesion. Heart not enlarged.
			Aug., 1915. Complaint and physical examination about same as last note. One enlarged gland at angle jaw on each side; not enlarged in posterior triangles. Sinuses clear. No recurrence of chorea.
			Oct., 1914. Choreiform movements ceased soon after leaving hospital; well for 3 months. Recurrence 1 month ago. Is undernourished; pale; very irritable. No colds or sore throat to which recurrence can be attributed.
			Feb., 1915. Admitted hospital with acute chorea and endocarditis. Heart enlarged; loud, rough systolic murmur at apex and transmitted to axilla and back. Blood culture negative.
			Mar., 1915. Choreiform movements persist. Heart smaller; otherwise as before. No arthritis.
			Aug., 1915. No chorea at present; very nervous, excitable and irritable. Throat looks normal. No sore throat since June, 1914.

TABLE VI.—REMOVAL OF TONSILS AND ADENOIDS FOR SYDENHAM'S CHOREA
II. CASES BETWEEN 6 AND 10 YEARS OF AGE—Continued.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion.	Special Examination.	Temp. (Mouth on Day Before Operation. ° F.
M. H. 35134. Female.	W	10	School.	Frequent tonsillitis for several years. Mouth-breather; very backward in school. Always a "nervous child." About 6 weeks ago twitching of arms, legs and face first noticed. No arthritis.	None.	Tonsils: Meeting in mid-line; left is particularly adherent to pillars. Nasopharynx: Large mass adenoids; adenoid facies; chronic discharge from nose; mouth-breather. Teeth: No note. Ears: Chronic catarrhal otitis media. Cervical glands: Slightly enlarged angles jaw. Tonsils: Not enlarged; adherent to pillars. Adenoids: Were removed in Feb., 1913. Ears: Normal; hearing good. Teeth: Carious. Cervical glands: Enlarged; measure about 2 x 5 cm. at angle jaw on each side.	98.6
M. D. 36561. Male.	W	9	School.	Frequent tonsillitis; mouth-breather; frequent earache; croup; cough for past 4 or 5 years. Acute mastoiditis with sinus thrombosis in Feb., 1913. First attack chorea followed this ear infection; gradually cleared up. No heart lesion; no arthritis. Is very nervous.	None.	Tonsils: Much enlarged; irregular surface; adherent to pillars. Teeth: Carious. Ears: Not infected. Nose: Normal. Nasopharynx: Large mass adenoids. Cervical glands: Enlarged in all triangles.	98.2
M. P. 34291. Female.	W	10	School.	History occasional tonsillitis; frequent "colds." Acute rheumatic fever 2 years ago; all joints swollen, red, very painful. Second attack rheumatic fever 4 months ago with involvement of all joints; pain around heart and shortness of breath. Was in bed for nearly 3 months. No history chorea.	Mitral insufficiency. Pericarditis with effusion.	Tonsils: Much enlarged; irregular surface; adherent to pillars. Teeth: Carious. Ears: Not infected. Nose: Normal. Nasopharynx: Large mass adenoids. Cervical glands: Enlarged in all triangles.	99.2

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

L. D. 28789. Male.	C	12		Epidemic meningitis in June, 1911; recovery without apparent injury to C. N. S. Acute tonsillitis at frequent intervals; attack 6 weeks ago followed by acute chorea; pericarditis; multiple arthritis; endocarditis.	Mitral insufficiency. Pericarditis.	Tonsils: Very large; crypts filled with foul smelling yellowish debris; adherent to pillars. Adenoids: Large mass; mouth-breather. Teeth: Two carious; others good. Nose: Normal. Ears: Normal. Cervical glands: Enlarged in all triangles; especially right.	99
J. M. 30923. Male.	W	11	School.	No history tonsillitis. In 1910 was in hospital with acute endocarditis and chorea. In Oct., 1912, was admitted with acute chorea, and polyarthritis. Was thought advisable to remove tonsils as a prophylactic measure.	Mitral insufficiency. Mitral stenosis?	Tonsils: Not enlarged. Adenoids: Very small amount. Nose: Clear; no sinus infection. Ears: Normal. Teeth: Excellent. Cervical glands: Just palpable.	99.4
C. C. 31049. Female.	W	15	School.	Frequent colds and sore throats for past 10 years. Mouth-breather. History chorea at intervals for several years. Is at present recovering from an attack of acute rheumatic fever with multiple arthritis and recurrence of chorea.	Mitral insufficiency.	Tonsils: Enlarged; adherent to pillars. Adenoids: Large mass; chronically infected. Teeth: Carious. Ears: Normal. Cervical glands: Enlarged in all triangles.	99
R. F. 31749. Male.	W	15	School.	Infrequent tonsillitis, but frequent cold in head. Chorea for 1 year; twitching of face, arms, legs. Unable to write as well as usual. No arthritis. Has choreiform movements of arms and face at present.	None.	Tonsils: Small; embedded; adherent. Nasopharynx: Large mass adenoids; discharge from nose and in throat. Ears: Normal. Nose: Deflected septum; no sinus infection. Cervical glands: Just palpable.	98.2
E. S. 32106. Female.	W	12	School.	No history tonsillitis, but child has frequent "colds," and swelling of glands neck. First attack chorea 6 months ago; cleared up 1 month ago. No arthritis.	None.	Tonsils: Small; adherent to pillars; fibrous. Teeth: Good. Nose: Hypert. inf. turb.; otherwise normal. Ears: Normal. Nasopharynx: Infected adenoids; discharge. Cervical glands: Enlarged slightly at angle jaws; not enlarged in posterior triangles.	98.4
D. S. 34202. Female.	W	11	School.	History of only one attack tonsillitis. Was operated on for empyema in this hospital 1 year ago; at that time heart was normal. Had chorea 6 months ago which has entirely disappeared. At this time was quite sick for several weeks. High fever. Was treated by family doctor. Was evidently acute endocarditis. No history arthritis.	Mitral insufficiency.	Tonsils: Much enlarged. Adenoids: Have been removed. Ears: Normal. Teeth: Good. Nose: No sinus infection. Cervical glands: Enlarged, particularly at angles jaw.	99
E. W. 34453. Male.	W	14	School.	History occasional sore throat; frequent colds. Has had two attacks chorea. The first attack chorea when 9 years of age; has had difficulty in articulating since this time. Is just recovering from the second attack. Legs, arms, face involved. No arthritis.	None.	Tonsils: Much enlarged; crypts filled with yellowish debris. Teeth: Very bad; alveolar abscesses. Adenoids: Have been removed. Nose: No sinus infection. Ears: Normal. Cervical glands: Large glands at angle jaw on right; enlarged in all triangles. Vocal cords: Move normally.	98.4
M. P. 37443. Female.	W	13	School.	History frequent tonsillitis. Following last attack had enlarged and tender glands neck; pain, stiffness, swelling of knees and ankles; jerking of muscles of arms and face. Onset about 5 week ago.	None.	Tonsils: Much enlarged; adherent. Nose: Septum dev. to left. Ears: Normal. Teeth: Carious. Cervical glands: Enlarged in all triangles.	98
D. B. 37442. Female.	W	15	School.	Frequent tonsillitis since early childhood. Tonsils "clipped" five times. Complains of general weakness, palpitation, loss appetite, and enlarged cervical glands. Choreia with palsy entire right arm and leg 2 years ago. At that time diagnosis mitral insufficiency was made by family physician.	Mitral insufficiency.	Tonsils: Enlarged; much scar tissue; very adherent to pillars. Adenoids: Small amount, chronically infected. Ears: Normal. Nose: Slight hypert. both inf. turbinates. Teeth: Good. Cervical glands: Much enlarged at angles jaw; less large in posterior triangles.	99

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

II. CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

General Physical Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative. Complications.	Subsequent Examination.
No general glandular enlargement. Heart: Normal. Lungs: Normal. Urine: Normal.	Aug., 1914. Chronic tonsillitis. Chorea.	None.	July, 1915. No recurrence of chorea. Better health than ever before; has gained 12 pounds; appetite good; "progress in school more rapid in past year than in previous 2 years." No colds or sore throats since operation. (Note.—Benefit probably due largely to removal of adenoids.)
No general glandular enlargement. Heart: Normal. Lungs: Impaired percussion note left apex; no râles. Tirquet: Negative. Urine: Normal.	Mar., 1915. Chronic tonsillitis. Cervical adenitis. Chorea. (Referred to dentist.)	None.	June, 1915. Glands at angle jaws measure $1\frac{1}{2} \times \frac{1}{2}$ cm. Teeth carious. Throat normal looking. Has attacks in which he becomes very pale, after which he lies down and sleeps for an hour or more. (Petit mal?) Feb., 1916. Recurrence chorea; palsy left arm and leg. In bed for 3 months; gradually cleared up. No heart or joint lesion.
General glandular enlargement. Heart: Enlarged to left and right. Systolic murmur transmitted to axilla and back. Lungs: General infiltration (X-ray). Very few physical signs. Urine: Normal aside from trace albumin. Liver: 2 cm. below c. m. Spleen: Palpable. R. B. C.: 4,000,000. W. B. C.: 15,600. Hb.: 50%. Culture from tonsils after removal. (Strep. hemolyticus.)	April, 1914. Chronic tonsillitis. Heart lesion. Pericarditis. Acute rheumatic fever. Secondary anæmia.	None.	Feb., 1915. Has had two attacks chorea since operation; none before operation. No recurrence of arthritis. Heart: Enlarged; dyspnoea. No friction rub heard. Aug., 1915. No recurrence of chorea. General health better than ever before. No evidence of arthritis. Heart: Well compensated. Has discharge from left ear of 1 week's duration; otherwise nose, throat, and nasopharynx normal. Hypertrophic pharyngitis.

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

Marked general glandular enlargement. Lungs: Clear on perc. and ausc. Urine: Normal aside from trace albumin. R. B. C.: 4,500,000. W. B. C.: 4500. Hb.: 75%. Blood culture negative.	Nov., 1911. Chronic tonsillitis. Chorea. Mitral insufficiency. Pericarditis.	None.	Mar., 1913. Patient died a week ago at his home. Apparently another acute attack rheumatic fever; had polyarthritis; great dyspnoea, etc. No autopsy.
Slight general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: Enlarged. Systolic murmur well transmitted. Presystolic thrill; crescendo late diastolic murmur. R. B. C.: 4,900,000. W. B. C.: 14,000. Hb.: 92%. Spleen enlarged. Blood culture negative.	Nov., 1912. No definite indication; was done as a prophylactic measure. Heart lesion. Chorea. Polyarthritis.	None.	June, 1915. No recurrence of arthritis; joints all normal. Still very nervous and jerky, particularly noticeable in writing; occasionally this jerking becomes much worse. Cervical, axillary and inguinal glands all slightly enlarged. Spleen not felt. Liver not enlarged. Heart: Left border is 7 cm. from median line; not enlarged to right. Systolic retraction at apex impulse. Sounds at apex and base are normal. No murmurs are heard, either systolic or diastolic.
General glandular enlargement. Spleen palpable. Lungs: Clear on perc. and ausc. Heart: Enlarged; definite mitral insufficiency. Urine: Clear. Thyroid: Enlarged.	Dec., 1912. Chronic tonsillitis. Heart lesion. Arthritis. Chorea. (Extraction carious teeth.)	None.	Nov., 1915. No recurrence of chorea. Arthritis cleared up in all joints except fingers and jaw; patient thinks these joints are gradually becoming worse. At present can eat only soft diet; teeth can be separated only about 1 cm. Heart: As before except it is smaller. Sinuses all clear on examination and X-ray.
No general glandular enlargement. Spleen not felt. Lungs and heart: Normal. Urine: Normal.	Mar., 1913. Chronic tonsillitis(?) Chorea.	None.	Nov., 1915. Still has twitching of muscles around eyes and forehead (looks like habit spasm); otherwise no evidence of chorea. Throat looks normal with exception chronic hypertrophic pharyngitis. No headache. Ears normal. Heart is normal.
No general glandular enlargement. Heart and lungs: Normal. Urine: Normal.	May, 1913. Chronic tonsillitis. Infected adenoids. Chorea.	None.	April, 1914. Has had three attacks of chorea since operation; all involve right arm and leg chiefly. General health improved; has gained in weight. No colds or sore throats. Throat looks normal. Cervical glands just palpable. Heart normal. Aug., 1915. Has had two attacks chorea since last note; still twitching of arms and legs. Very irritable, restless and nervous. Nose, throat, ears, cervical glands all normal. No evidence of cardiac involvement.
General glandular enlargement. Spleen enlarged. Lungs: Evidence of old empyema trouble. Heart: Enlarged to left; definite mitral lesion. Urine: Clear. W. B. C.: 9200. Hb.: 85%.	Mar., 1914. Chronic tonsillitis. Heart lesion. Chorea.	None.	Feb., 1915. No recurrence of chorea. Frequent colds, cough, expectoration (bronchiectosis?). Oct., 1915. General health much improved. Cervical glands not palpable. Throat looks normal. Heart: Left border heart 8.2 cm. left median line; right is $1\frac{1}{2}$ cm. to right median line. Blowing systolic murmur at apex, transmitted into axilla. Pulse 72, regular. Thyroid enlarged. No recurrence of chorea.
Slight general glandular enlargement. Heart and lungs: Normal. Urine: Clear. Culture from tonsils after removal. (Staphylococci.)	April, 1914. Chronic tonsillitis. Chorea. (Extraction infected teeth.)	None.	May, 1914. Chorea much worse than at time of operation. Oct., 1915. Chorea not improved. Speech difficulty; twitching legs and arms. Cervical glands not palpable. Teeth in poor condition. Chronic pharyngitis. Nose, nasopharynx, sinuses and larynx all look normal.
Slight general glandular enlargement. Heart and lungs: Normal. Urine: Normal.	July, 1915. Chronic tonsillitis. Cervical adenitis. Infectious arthritis. Chorea.	None.	Nov., 1915. No recurrence of chorea. All joint symptoms have cleared up entirely. No sore throat or coryza since operation. Glands in anterior and posterior triangles are not palpable. Throat and nasopharynx look normal. Oct., 1916. No recurrence of chorea. Cervical glands not palpable. General health good. Gaining in weight.
No general glandular enlargement. Heart: Enlarged to left; systolic murmur of greatest intensity at apex; transmitted to axilla and back. Lungs: Clear on perc. and ausc. Urine: Normal. Liver and spleen: Not enlarged.	July, 1915. Chronic tonsillitis. Cervical adenitis. Heart lesion. Chorea.	None.	Nov., 1915. No recurrence of chorea. General health much improved. Cervical glands are not palpable in either anterior or posterior triangles. Throat looks normal aside from hypertrophic pharyngitis. Nasopharynx and nose: Normal. Heart: Smaller; well compensated; otherwise as before. Nov., 1916. No recurrence of chorea.

TABLE VII.—RENAL GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR NEPHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion. Arthritis.	General Physical Examination.	Special Examination. Nose, Throat, Ears and Sinuses.
G. P. 29943. Female.	C	8		Following very severe tonsillitis and acute otitis media 8 months ago the cervical glands rapidly enlarged and suppurated. Shortly after this began to have headaches, abdominal pains, vomiting, swelling ankles and under eyes. Scars of old tbc. fistula on left side neck. History frequent tonsillitis and coryza.	Mitral insufficiency. Tbc. arthritis left heel.	Ill looking, anæmic, poorly nourished. Edema ankles, face. Heart: Enlarged; mitral lesion. Lungs: Clear on perc. and ausc. aside from bronchial rales. Blood pressure: 125 mm. Hg. Blood: R. B. C., 3,200,000; W. B. C., 12,600; Hb., 40%. Temperature (evening) 100.2° F. Retrosternal dullness due to thymus or glands.	Tonsils: Enlarged; adherent to pillars; no ulceration. Adenoids: Very large; mouth-breather. Ears: Chronic suppurative otitis media right (possibly Tbc.). Teeth: Good. Nose: Normal aside from discharge; no sinus infection. Cervical glands: Typically tuberculous. (Microscopic examination: Tonsils after removal showed no tbc. lesion; adenoid sections lost.)
E. T. 32512. Female.	W	6		Comes to dispensary on account of frequent tonsillitis with high fever; mouth-breather; and enlarged glands on right side neck. No history of scarlet fever; always well aside from above trouble.	None.	General glandular enlargement. Cervical glands especially large at angle jaws. Heart and lungs: Clear. Eye grounds: Normal.	Tonsils: Much enlarged; adherent. Adenoids: Much enlarged; mouth-breather. Ears: Chronic catarrhal otitis media. Teeth: Carious. Cervical glands: Prominent on inspection at angle jaw left measure 4 x 5 cm.
L. J. 37474. Male.	W	10		Is recovering from an attack of acute tonsillitis which was followed by acute nephritis and multiple arthritis. History headaches, vomiting, swelling face and ankles; and swelling, pain, stiffness of all joints, particularly knees, with above attack. Patient was treated by family physician; referred now for tonsillectomy. Never had scarlet fever.	No heart lesion. Multiple arthritis.	Walks with difficulty due to swelling in both knee joints; fingers also involved. Temperature 99° F. Throat still sore in A. M. Difficulty in breathing through nose. Heart: Slightly enlarged; systolic murmur over entire precordium; soft; not well transmitted. Lungs: Clear on perc. and ausc. Eye grounds normal. W. B. C.: 16,000. Hb.: 90%. Blood pressure 95 mm. Hg.	Tonsils: Enlarged; adherent. Adenoids: Large mass; infected. Ears: Chronic suppurative otitis media left. Teeth: Carious. Cervical glands: Enlarged at angle jaws, and in posterior triangles.
S. S. 33957. Male.	W	12		Frequent attacks tonsillitis; chronic nasal discharge; mouth-breather. Is just recovering from an attack of acute nephritis. Had edema face, legs. Vomiting and abdominal pain.	None.	General glandular enlargement. Heart: No lesion; slightly enlarged. Blood pressure: Hypertension. Lungs: Clear on posterior and anterior. R. B. C.: 4,100,000. W. B. C.: 8200. Hb.: 57%. Wassermann and Calmette: Negative.	Tonsils: Small; embedded; densely adherent to pillars. Adenoids: Large mass. Teeth: Fairly good. Ears: Normal. Cervical glands: Enlarged in anterior and posterior triangles.
J. M. 34062. Male.	W	16	Box factory.	Frequent tonsillitis; impaired hearing right ear 4 years. Chronic nasal discharge. No scarlet fever. Facial palsy acute right. (Was advised 4 years ago to have tonsils removed on account frequent tonsillitis.)	None.	Heart and lungs: Negative. Blood pressure 114 mm. Hg. Wassermann: Negative. Lumbar puncture: Negative. Retinitis.	Tonsils: Enlarged. Adenoids: Large mass. Ears: Chronic otitis media. Cervical glands: Enlarged on both sides angle jaw.
L. T. 35493. Male.	W	16	School.	Frequent tonsillitis; frequent colds. Comes to dispensary on account nasal obstruction and nasal deformity due to injury. Has frequent nose bleeds. Never had scarlet fever.	None.	Lungs: Clear on perc. and ausc. Heart: Slightly enlarged; systolic blow, not transmitted. Liver and spleen not palpable. W. B. C.: 9800. Hb.: 95%. Evening temperature 99° F. Blood pressure 120 mm. Hg.	Tonsils: Small; imbedded; very adherent to pillars. Adenoids: Large mass. Ears: Not infected. Teeth: Pyorrhœa; caries. Cervical glands: Markedly enlarged at angle jaws on both sides. Nose: Deflected septum due to fracture no sinus infection.
N. S. 36690. Male.	W	17		No history tonsillitis, but frequent "colds." Onset 4 days ago with fever, chills, pain in back and abdomen, vomiting, headache. Referred from medical department after 2 months in bed. Temperature still elevated in evening to 100 or 100.5° F.	None.	Lungs: Clear on perc. and ausc. Heart: Normal. Fund: Normal. R. B. C.: 5,300,000. W. B. C.: 5000. Hb.: 80%. Calmette and Wassermann: Negative. General glandular enlargement.	Tonsils: Small; densely adherent to pillars. Marked chronic hypertrophic pharyngitis. Adenoids: Small; chronically infected mucopurulent discharge. Ears: Not infected. Cervical glands: Enlarged at angles jaw smaller but definitely enlarged in posterior triangles.
R. R. 36881. Male.	W	12		Frequent tonsillitis. Chorea 5 years ago; affected arms; none for past 2 years. Frequent swelling glands neck. No history scarlet fever.	Mitral insufficiency. No arthritis. (Chorea.)	Heart: Enlarged to left; mitral insufficiency. Lungs: Clear on perc. and ausc. Pulse: Regular. Blood pressure: 110 mm. Hg.	Sinuses: Not infected. Tonsils: Enlarged; especially left. Adenoids: Large mass. Ears: Chronic otitis media left. Sinuses: Clear. Teeth: Carious. Cervical glands: Enlarged.
R. McA. 38210. Male.	W	19	Clerk.	History occasional tonsillitis. Blood accidentally discovered in urine. No headaches; no edema; vision good; patient attributes onset to "malarial fever." Hematuria first noted 6 years ago. No history scarlet fever. No pain in back or legs.	None.	No general glandular enlargement. Heart and lungs: Normal. No evidence of malaria or of malarial organisms. Blood pressure: 125 systolic; 80 diastolic. R. B. C.: 4,800,000. W. B. C.: 20,000. Hb.: 80%. Differential count shows 82.5% P. m. n.	Tonsils: Small; embedded; adherent to pillars. Abscess at lower pole left tonsil discovered at operation. Adenoids: Small; chronically infected discharge. Nose: No sinus infection. Ears: Normal. Teeth: Good. Cervical glands: No note.
T. M. 31038. Male.	W	47	Business.	Acute rheumatic fever at 16 and again at 25 years age. After last attack tonsils were "clipped" and for 20 years has been free from sore throat until present illness. Onset 10 months ago with acute tonsillitis, multiple arthritis and hematuria. After several months in Florida gradually improved. Another tonsillitis 3 months ago caused recurrence; and a third tonsillitis 1 month ago has made him much worse. Large sediment of blood in each voiding; practically all joints involved.	No heart lesion. Multiple arthritis.	Slight general glandular enlargement. Lungs: Clear on perc. and ausc. Heart: No organic lesion. Joints: Swollen, painful on motion. Blood pressure 120 mm. Hg. Eye grounds normal. Wassermann: Negative. Culture from tonsils after removal: Strep. viridans. (Green on blood agar. Coagulates milk. No capsule after passing through rabbits and mice.)	Tonsils: Slightly enlarged; densely adherent to pillars. Teeth: Not infected (X-ray). Nose: Chronic ethmoiditis right. Ears: Normal. Cervical glands: Enlarged and tender at angles jaw—particularly on right.
W. D. 32047. Male.	W	25	Student.	No history sore throat, or of frequent coryza. Tonsils partially removed 12 years ago. No symptoms of nephritis. Albumin, casts, blood found accidentally during examination for life insurance. No history scarlet fever.	None.	No general glandular enlargement. Heart: Systolic murmur mitral area; not enlarged. Lungs: Clear on perc. and ausc. Liver and spleen: Not palpable.	Tonsils: Small; imbedded; densely adherent to pillars; chronic abscess pocket at lower pole left tonsil. Adenoids: Large mass; infected. Ears: Normal. Teeth: Good (X-ray). Cervical glands: Enlarged at angles jaw especially on right.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.

Urinary Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Albumin: 5.5 gm. to liter. Casts: Many granular and blood. W. B. C. and R. B. C. Acid: 1013 sp. gr. Phthalein: 40% in 2 hours. Lactose: 24% in 4 hours; excretion completed 10 hours.	May, 1912. Frequent tonsillitis. Mouth-breather. Suppurated tbc. glands neck. Nephritis. Secondary anæmia. Heart lesion. (Incision, drainage tbc. glands neck.)	Temperature to 104° F. Gradually became normal. No change in urinary symptoms.	Patient died with acute nephritis in April, 1915.
Albumin: Trace. Casts: Granular and hyaline. Blood: None. No functional tests made.	July, 1913. Chronic tonsillitis. Cervical adenitis. Nephritis? (Referred to dentist.)	None.	Sept., 1915 (over 2 years after operation). General health excellent; has grown rapidly. No history of any of the symptoms of nephritis. No sore throat since operation; breathes normally. No headache. No general glandular enlargement. Cervical glands just palpable in anterior triangles; not enlarged in posterior triangles. Throat looks normal. Urine: Normal. No casts found.
Albumin: Large amount. Casts: Granular; hyaline; leucocyte. A few R. B. C. No functional test made.	July, 1915. Frequent tonsillitis. Mouth-breather. Otitis media. Cervical adenitis. Acute nephritis. Polyarthritis.	None.	Nov., 1915 (4 months after operation). Urine acid; faint trace albumin; sugar none; casts none; few red blood cells. Joints all normal. Heart: 2 cm. to right in 4 i. s.; to nipple line on left. Sounds clear. Pulse 80, regular. Lungs: Clear. Spleen not palpable. Cervical glands: On left at angle jaw measures 1 x 2 cm.; discrete; hard; movable. Smaller in other triangles. Still some carious teeth (referred to dental department). Drums intact; hearing good. Nov., 1916. Urine: Clear; sp. gr. 1022; acid; no sugar; no albumin; no casts; no R. B. C. General health is good.
Sp. gr. 1010 to 1020. Albumin: Large amount. Casts: Finely granular and blood. W. B. C. and W. B. C. Uiac: Positive. Phthalein: 2 hours 70%; 1st hour 50%; 2d hour 20%. Lactose: Delayed excretion; trace in 7 hours.	Feb., 1914. Frequent tonsillitis. Mouth-breather. Nephritis.	None.	April, 1915 (over 1 year after operation). Urine normal in every way. Heart slightly enlarged; otherwise normal. Blood pressure 110 mm. Hg. No general glandular enlargement. Cervical glands barely palpable. No illness of any kind since operation; no recurrence of swelling of face or ankles; no headache or vomiting. Eye grounds normal. Aug., 1915. Is still perfectly well. Urine normal. (Referred to dental clinic.) Aug., 1916. Urine examination: Clear; acid; sp. gr. 1010; no albumin; no sugar; Ep. cells and a few W. B. C. No casts or R. B. C. Subjectively is perfectly well.
Albumin: Present (2 gm. liter). Casts: Granular; leucocyte. W. B. C. and W. B. C. Uiac: Positive. Phthalein: 60% 1st hour; 10% 2d hour. Lactose: 46% in 2 hours. Albumin: 1.3 gm. to liter. Casts: Granular and leucocyte. No red blood cells seen. Uiac: Negative. Phthalein: 1st hour 60%; 2d hour 10%.	April, 1914. Chronic tonsillitis. Chronic nephritis. Oct., 1914. Chronic tonsillitis. Cervical adenitis. Nephritis. (Nasal operation also.)	None. None.	Aug., 1916 (over 2 years after operation). Subjectively is perfectly well. Works regularly in box factory for past 1½ years. Vision good. No headaches. Urine: Clear; acid; 1015; albumin trace; sugar 0; no casts or R. B. C. found. Aug., 1915. Urine: No albumin; no sugar; no casts, leucocytes or red blood cells. Lungs, heart, abdomen negative. Has had no sore throat or cold since operation. Eye grounds normal.
Sp. gr. 1030. Albumin: Large amount. Casts: Granular, blood, leucocyte. Phthalein: 75% in 2 hours.	May, 1915. Chronic tonsillitis. Chronic nasopharyngitis. Nephritis. (Referred to dentist.)	None.	Dec., 1915. Urine: No albumin; no sugar; no casts of any kind; no R. B. C. or W. B. C. Patient states that he has been in perfect health for past 6 months. Cervical glands are barely palpable. Throat and nasopharynx look practically normal; no discharge; chronic pharyngitis possibly due to smoking. (Again referred to dentist.)
Albumin: Present. Casts: Present. W. B. C. and R. B. C.	June, 1915. Chronic tonsillitis. Nephritis.	None.	Aug., 1916. Perfectly well. No recurrence chorea. No cardiac or renal symptoms. Urine: Sp. gr. 1010; acid; albumin 0; sugar 0; casts 0; no R. B. C. (Normal in every way.) Heart: P. M. I. in 4 s. 7 cm. left mid-line. There is a soft systolic murmur heard all over heart, loudest at apex. Not transmitted to axilla and back as in June, 1915. Throat, teeth, nose, ears all look normal. Cervical glands just palpable.
cystoscopic examination showed blood coming from both kidneys, but more from right. No stone. bacteriological examination: Negative. Sp. gr. 1020. Albumin: Trace. Many R. B. C.; few W. B. C. Phthalein (4 different tests): 1st hour 18 to 20%; 2d hour 18 to 20%. Food urea .828 per 1000 cc.	Oct., 1915. Chronic tonsillitis. Hematuria.	None.	Oct., 1915. Within a week after the operation the amount of blood in urine has markedly decreased. May, 1916. Very small amount blood in urine; no longer evident on macroscopic examination. Has gained 26 pounds in weight. General health better than ever before.
bacteriological examination negative. ray kidneys negative. Albumin: Large amount. Casts: Granular and R. B. C.; few W. B. C. Blood: Large sediment in each voiding. No functional test.)	Dec., 1912. Chronic tonsillitis. Chronic ethmoiditis. Multiple arthritis. Hematuria. (Nasal operation also.)	None.	Dec., 1912. Within a few days after the tonsillectomy there was an acute flare-up of the arthritis, but at the same time an improvement in the urinary condition. Dec., 1913. Joints steadily improved after this last acute attack in Dec., 1912; have been normal in every way for the past 8 or 9 months. General health good. Blood pressure 120 mm. Hg. Urine: Slight trace albumin; a few hyaline casts; 7 to 10 red blood cells in microscopic field of centrifuge spec., while 1 year ago there were 400 or more in a field of a plain specimen. Mar., 1916. In perfect health. Joints normal. Urine normal in every way.
amination genito-urinary tract negative. ray kidneys: Negative. Albumin: Large amount. Casts: R. B. C. and W. B. C.; hyaline and finely granular. Phthalein excretion: 64%.	April, 1913. Chronic tonsillitis. Infected adenoids. Cervical adenitis. Nephritis.	None.	May, 1913 (1 month after operation). Albumin 1 gm. to liter; number casts less. General condition excellent. July, 1914. Trace of albumin; but very few casts, R. B. C. or W. B. C. now found in centrif. specimen. Nasopharynx and throat look normal. Oct., 1915. Still trace albumin. All casts, blood and pus disappeared in May, 1915. Blood pressure 130 mm. Hg. Works on farm regularly for past 2 years.

TABLE VII.—RENAL GROUP. REMOVAL OF TONSILS AND ADENOIDS FOR NEPHRITIS

Name. Surg. No. Sex.	Race.	Age.	Occupation.	History.	Heart Lesion. Arthritis.	General Physical Examination.	Special Examination. Nose, Throat, Ears and Sinuses.
E. McC. 33944. Med. Female.	W	21	School.	Occasional sore throat, especially in A. M. No acute tonsillitis for several years. Easily tired; loss appetite; frequent nausea. No headache. No history scarlet fever.	None.	No general glandular enlargement. Gastric analysis: Free Hcl. 26%; total acidity 50%. Heart and lungs: Normal. Ptosis abdominal organs. W. B. C.: 7600. Hb.: 70%.	Tonsils: Embedded; small; densely adherent. (Have been partially removed. Adenoids: Small amount. Teeth: Wisdom infected on right (X-ray). Ears: Normal. Cervical glands: Enlarged, tender angles jaw; especially on right. Sinuses: Not infected.
A. P. 34434. Female.	W	36	Housewife.	Frequent tonsillitis every winter since childhood. Headache, impaired hearing and tinnitus for past year. Nycturia for past year. No scarlet fever.	Mitral insufficiency.	Heart: Enlarged; mitral insufficiency. General arteriosclerosis. Blood pressure: 220 systolic; 140 diastolic.	Tonsils: Enlarged; adherent. Adenoids: Enlarged. Teeth: Pyorrhea; caries. Cervical glands: Evident on inspection angles jaw.
A. McL. 34690. Male.	W	30	Minister.	Frequent tonsillitis. Has had five attempts to remove tonsils. Constant discharge in throat. Albumin and blood in urine discovered 5 years ago during examination for life insurance. Headache frequent. Vision good. No history scarlet fever.	None.	No general glandular enlargement. Heart and lungs: Normal. Temperature at present 99.8° F. Liver and spleen: Not palpable. Wassermann: Negative. Genito-urinary examination: Negative.	Tonsils: Embedded; fibrous; densely adherent to pillars. Adenoids: Enlarged; chronically infected discharge in nasopharynx. Nose: Hypert. inf. turb.; sinuses all clear. Ears: Chronic catarrhal otitis media. Cervical glands: Much enlarged at angles jaws; tender; slightly enlarged at posterior triangles. Teeth: Abscess upper bicuspid on right.
S. S. 35372. Male.	W	21	Laborer.	History one severe attack tonsillitis 5 years ago; was in bed 2 or 3 weeks. No sore throat since. Referred from medical department where he has been treated for acute nephritis. Has headache, pain in back and abdomen, vomiting, generalized edema.	None.	No general glandular enlargement. Heart: Slightly enlarged; no organic lesion. No special thickening of vessel walls. Lungs: Clear on perc. and ausc. Blood pressure 150 mm. Hg. R. B. C.: 5,008,000. W. B. C.: 10,000. Hb.: 85%. Temperature 100° F.	Tonsils: Small; imbedded; densely adherent to pillars. Adenoids: Small; infected. Nose: Hypert. inf. turbinates; no discharge; X-ray shows clouding left antrum; no pus on irrigation. Teeth: Pyorrhea; caries. Ears: Chronic catarrhal otitis media. Cervical glands: Enlarged; tender angles jaw; especially left.
H. M. R. 32274. Male.	W	29	Physician.	Chorea when a child. Frequent tonsillitis. Tonsils were partially removed on two occasions. Severe tonsillitis 1 year ago, another attack 1 month before present illness. This latter attack was due to streptococcus. After acute symptoms subsided had headache, general malaise, loss appetite. After 3 weeks friend noticed swelling face. Urine then found to contain large amount albumin, casts and blood. About same time joints became swollen and painful.	No heart lesion. Multiple arthritis.	General Glandular enlargement. General edema. Joints swollen, painful; not red. Heart: Normal. Lungs: Normal. Wassermann: Negative.	Tonsils: Enlarged; densely adherent to pillars. Adenoids: Small amount. Teeth: Poor, caries and pyorrhea. Nose: No sinus infection. Ears: Normal. Cervical glands: Barely palpable though quite tender. (Patient quite fat.)
G. B. 37901. Female.	W	26	Nurse.	Frequent tonsillitis and quinsy. Tonsillitis 2 months ago very severe; followed by multiple arthritis and acute nephritis. The edema has all cleared up, but albumin, casts and dimin. output continue.	No heart lesion. Multiple arthritis.	Slight general glandular enlargement. Heart: Normal. Lungs: Normal. Joints: Still stiff and painful after exercise.	Tonsils: Slightly enlarged; densely adherent to pillars. Right larger than left (due to quinsy?). Adenoids: Small amount. Teeth: Good. Ears: Not infected. Nose: Sinuses clear.
C. W. 31435. Male.	W	16	Laborer.	History frequent tonsillitis since early childhood. Acute rheumatic fever in Dec., 1912. Ankles and knees still stiff and painful. Also had hematuria for first time in Dec., 1912. Is just recovering from a second attack of rheumatic fever.	Mitral insufficiency.	Slight general glandular enlargement. Lungs: Clear. Heart: Enlarged; mitral insufficiency. Spleen: Palpable; enlarged. R. B. C.: 4,500,000. W. B. C.: 9500. Hb.: 80%.	Tonsils: Enlarged; adherent. Adenoids: Enlarged. Teeth: Caries. Nose: Sinuses clear. Cervical glands: Visibly enlarged at angles of jaw.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT. I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
R. B. 29823. Female.	W	4	Frequent sore throat, chills and fever for 1 year. Mouth-breather. Difficulty in swallowing.	Enlarged at angle jaw and in posterior triangles. Both submaxillaries enlarged.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Excellent.	Normal. W. B. C.: 8400. Hb.: 74%. Temperature: 99.4° F.
E. M. 31007. Female.	W	5	Mouth-breather; frequent colds. Recently two severe attacks tonsillitis.	Enlarged in anterior triangles.	Adenoids: Large mass. Tonsils: No note on size.	Normal. Temperature: 98.6° F.
M. E. 31299. Male.	W	3	Swelling glands neck. Mouth-breather. Frequent colds.	Size hickory-nuts at angle jaw on each side.	Tonsils: Slightly enlarged. Adenoids: Very large. Teeth: Good.	Normal. Temperature: 98.6° F.
M. H. 31450. Female.	W	3	Frequent sore throat; fever, swelling glands neck; speech thick.	Glands at angles jaw evident on inspection; hard, movable.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Good.	Normal. W. B. C.: 8400. Temperature: 99° F.
H. C. 31590. Female.	C	5	Swelling glands neck; frequent sore throat; mouth-breather.	Very large; hard; movable in both anterior triangles.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Good.	Normal. W. B. C.: 9900. Hb.: 75%. Temperature: 99° F.
M. G. 31663. Male.	W	5	Frequent attacks tonsillitis.	Enlarged at angles jaw and slightly in posterior triangles.	Tonsils: About normal size. Adenoids: Large mass. Teeth: No note.	Normal. Temperature: 99.6° F.
J. L. 31864. Male.	W	3	Mouth-breather; fretful; poor appetite.	Very large at angles jaw, suggest tubercle glands.	Tonsils: Very large. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 99° F.
L. R. 32006. Female.	W	2	Swelling glands angles jaw; impairment hearing; difficulty in swallowing.	Size hickory-nuts on both sides at angle jaw.	Tonsils: Meet in mid-line. Adenoids: Very large. Ears: Slight discharge both sides. Teeth: Good.	Normal. W. B. C.: 11,000. Hb.: 75%. Temperature: 99° F.

WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.

Urinary Examination.	Date and Indication for Operation. Tonsillectomy.	Post-operative Complications.	Subsequent Examination.
Albumin: Trace. Casts: Many hyaline, finely granular, and leucocyte. Few red blood cells.	April, 1915. Chronic tonsillitis. Cervical adenitis. Nephritis. (Extraction wisdom tooth right.)	None.	Dec., 1915 (8 months after operation). Urine examination normal on two different days. No albumin; no casts; no blood. Has gained 40 pounds in weight. No longer any nausea; appetite good. General health better than ever before.
Sp. gr. 1018; acid. Albumin: 1 gm. to liter. Sugar: 0. Casts: Granular.	April, 1914. History frequent tonsillitis. Chronic nephritis. Arteriosclerosis.	None.	April, 1916. Died pneumonia. During past 2 years was admitted to hospital on three occasions for nephritis. The tonsillectomy was of no apparent benefit. Autopsy showed chronic diffuse nephritis; general arteriosclerosis; cardiac hypertrophy; albuminuric retinitis; and cerebral hemorrhage right.
Albumin: Heavy trace. Blood: Large sediment with each voiding. Casts: Few hyaline and finely granular.	June, 1914. Chronic tonsillitis. Infected adenoids. Nephritis. (Referred to dentist.)	None.	Dec., 1914. No blood, pus or casts in urine; trace albumin. Gained 10 pounds in weight. Oct., 1915. Has had five examinations of urine since last report, all normal with one exception. After returning from a strenuous hunting trip a trace of albumin was found, but no blood or casts. General health excellent. No headaches. Appetite good.
Albumin: Large amount. Casts: Blood, leucocyte, granular in large numbers. Large sediment blood in each voiding. Uthalein: June, 1914, 25%; Sept., 1914, 64%. At time of operation edema had cleared up and urine contained less blood and albumin than above report.)	Sept., 1914. Chronic tonsillitis. Infected adenoids. Nephritis. (Referred to dentist.)	None.	Sept., 1915. Urine: Sp. gr. 1020; no albumin (nitric acid or heat and acetic); no sugar; no casts of any kind after centrifugalizing. Blood pressure 125 mm. Hg. Heart: 12 cm. to left; 3½ cm. to right; no murmurs. Lungs clear. General condition excellent. Works regularly. Glands at angle jaws not palpable; a few small glands in posterior triangles. Teeth: Still in bad condition (again referred dental department). Nose: Looks normal.
Albumin: 5 grams to liter. Casts: Blood, leucocyte, granular. Uthalein: 44% in 2 hours.	June, 1913. Chronic tonsillitis. Acute nephritis. Acute arthritis following attack tonsillitis. (Referred to dentist.)	None.	Aug., 1916. Urine: Clear; acid; 1010; albumin 0; sugar 0; no casts or R. B. C. found. Subjectively perfectly well; works regularly.
Albumin: Heavy trace. Casts: Hyaline; granular. Few R. B. C.; much less than a month ago.	Sept., 1915. Chronic tonsillitis. Nephritis. Polyarthrititis.	Temporary increase in albumin, casts and joint symptoms.	Nov., 1914. Urine completely cleared up within 6 months after operation. Joints all normal. General health excellent. April, 1916. Urine normal in every way. Joints normal.
Albumin: Heavy trace. Casts: Granular, hyaline, blood and leucocyte. Blood: Large sediment.	Feb., 1913. Chronic tonsillitis. Acute rheumatic fever. Endocarditis. Nephritis.	None.	June, 1916. Urine normal in every way. Joints normal. General health excellent. Sept., 1916. Urine normal in every way. Joints normal.
			Aug., 1916. Urine: Acid, sp. gr. 1007; albumin 0; sugar 0; one granular cast found. Subjectively is perfectly well. Working regularly for past two years. Joints normal. Has had no recurrence of rheumatic fever. Heart: Definite mitral insufficiency.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.
I. CASES BETWEEN 1 AND 5 YEARS OF AGE.

Date and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
May, 1912. Chronic tonsillitis. Cervical adenitis. Mouth-breather.	None.	Aug., 1915. Excellent.	One gland angle jaw palpable on right; about ½ cm. diameter. Shot-like glands posterior triangles.	Teeth: Carious molar right. Throat, nose, ears: Normal.	Well.
Nov., 1912. Chronic tonsillitis. Cervical adenitis. Mouth-breather.	None.	May, 1913. Still mouth-breather. Fewer colds. June, 1915. Is perfectly well.	At angle jaw on right enlarged; on left not palpable. Gland on right still enlarged. Submaxillary glands not palpable.	Teeth: Good. Throat, nose, ears: Normal.	One small gland on right still palpable.
Jan., 1913. Enlarged cervical glands. Mouth-breather.	None.	July, 1915. Grown rapidly. Has frequent colds. Pain in left ear at times; no discharge.	At angle jaw on each side ½ cm. diameter. Small in posterior triangles.	Teeth: Carious. Nose and throat: Normal. Ears: Chronic catarrhal otitis media.	Glands almost disappeared.
Feb., 1913. Cervical adenitis. Speech impaired. Mouth-breather.	None.	May, 1913. Much improved. April, 1914. Perfectly well. Sept., 1915. Perfectly well.	Gland on left just palpable. Gland on left just palpable. Just palpable in anterior and posterior.	Throat: Looks normal. Hypert. nodules lymphoid tissue on pharynx wall.	Well.
Feb., 1913. Cervical adenitis. Mouth-breather.	None.	Aug., 1915. No colds or other illness since operation.	Glands not palpable in anterior triangles on either side.	Teeth: Good. Throat: Hypert. lymphoid tissue on pharynx wall.	Well. Glands not palpable, although alveolar abscess. Still present.
Mar., 1913. Chronic tonsillitis. Cervical adenitis.	None.	April, 1914. Much improved. No colds. Grown rapidly.	Glands just palpable at angle jaws and in posterior triangles.	Teeth: Alveolar abscess upper bicuspid left. Throat, nose, ears: Normal.	Well.
April, 1913. Cervical adenitis. Mouth-breather.	None.	April, 1914. No gain in weight. Appetite poor. Mouth-breather. No colds since operation. Aug., 1915. Much improved in last year. Mouth closed.	At angle jaw on right one gland about 1 cm. diameter; smaller on left. Glands size small shot in anterior and posterior triangles.	Teeth: Four carious. Ears: Normal. Teeth: Still carious. Lymphoid hyperplasia pharynx.	Well.
April, 1913. Cervical adenitis. Chronic otitis media.	None.	Aug., 1915. Excellent since operation. Ears normal. Has grown rapidly.	Still slightly enlarged angle jaw left. Not palpable on right.	Teeth: Good. Throat: Normal looking. Ears: Normal looking.	Well.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT.

I. CASES BETWEEN 1 AND 5 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
F. B. 32320. Male.	W	4	Swelling glands neck; frequent sore throat; mouth-breather; difficulty in swallowing.	Enlarged at angles of jaw and in posterior triangles.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 99° F.
W. G. 32492. Male.	W	5	Frontal headache; frequent colds; mouth-breather.	Evident on inspection at angle jaws; hard; movable.	Tonsils: Much enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 98.2° F.
C. M. 33142. Male.	W	4	Frequent sore throat with fever; swelling glands neck noticed for 3 months.	Large mass hard, movable glands at angle jaw on each side.	Tonsils: Much enlarged. Adenoids: Large amount. Teeth: Carious.	Normal. No general glandular enlargement. W. B. C.: 14,500. Hb.: 95%. Temperature: 98° F.
E. C. 33217. Male.	W	2	Swelling glands neck noticed for 9 months; frequent colds; frequent earache; mouth-breather. Poor appetite; fretful.	Evident on inspection at angle jaws; hard; movable.	Tonsils: Enlarged; nodular. Adenoids: Large mass. Ears: Chronic discharge on left. Teeth: Good.	Normal. No general glandular enlargement. Temperature: 99° F.
M. F. 33309. Female.	W	5	Frequent sore throat; mouth-breather.	Slightly enlarged at angle jaws and in posterior triangles.	Tonsils: Enlarged. Adenoids: Enlarged; mouth-breather. Teeth: Carious.	Normal. W. B. C.: 12,800. Hb.: 85%. Temperature: 99° F.
A. W. 33436. Male.	C	5	Chronic cough; loss weight; poor appetite; chronic cold in head. "Suspicious pulmonary Tbc." (Medical department.)	Much enlarged; hard; movable at angle jaws.	Tonsils: Slightly enlarged; adherent. Adenoids: Large mass. Teeth: Good. Ears: Normal.	Impairment l. apex; rales over both lungs. W. B. C.: 15,200. Hb.: 60%. General glandular enlargement. Temperature: 99° F.
J. L. 33551. Male.	W	5	Frequent sore throat; enlarged cervical glands. Had diagnosis of Tbc. when 18 months of age. Uncle recently died Tbc. in same house.	Evident on inspection at angle jaws; hard; movable.	Tonsils: Much enlarged. Adenoids: Large; adenoid facies. Teeth: Carious.	Lungs and heart: Normal. Slight general glandular enlargement. Temperature: 98.6° F. Pirquet positive Oct., 1909.
V. B. 33669. Female.	W	3	Mouth-breather.	Slightly enlarged and hard at angle each jaw.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. W. B. C.: 7200. Temperature: 99° F.
H. W. 34491. Male.	C	2½	Chronic cough; difficulty in swallowing; swelling glands right side neck for one year.	Large mass glands at angle jaw right, and in posterior triangle right. Hard; adherent; fixed.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Good.	Lungs: Normal. Spleen: Not palpable. Heart: Normal. Temperature: 98.6° F.
K. P. 34572. Male.	W	4	Frequent sore throat; severe attack 1 month ago. Mouth-breathing. Loss appetite.	Slightly enlarged at angle jaws; discrete; hard.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Good.	Normal. W. B. C.: 11,500. Hb.: 70%. Temperature: 99.4° F.
E. L. 34614. Male.	W	5	Cold in head; frequent sore throat; mouth-breather.	Enlarged at angle jaws and in posterior triangles; discrete; hard.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98.6° F.
L. S. 34810. Male.	W	2	Fretful; cough; frequent colds; mouth-breather.	Enlarged at angle jaws; hard.	Tonsils: Enlarged, especially left. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 98.6° F. No general glandular enlargement.
V. H. 35042. Female.	W	4	Frequent sore throats; earache; mouth-breathing.	Markedly enlarged at angle jaws on both sides.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Carious. Ears: chronic otitis media supp.	Normal. Temperature: 99° F. No general glandular enlargement.
C. K. 35095. Male.	W	2½	Frequent earache with discharge; mouth-breather. Swelling glands neck for 6 months.	Large masses glands at angle jaw on each side; very evident on inspection; soft; not adherent.	Tonsils: Small; adherent to pillars. Adenoids: Large mass. Teeth: Good. Ears: Chronic otitis media.	Normal. R. Temperature: 99.6° F. No general glandular enlargement. Von Pirquet: Not positive.
H. D. 35901. Male.	W	2	Chronic cough 6 months; mouth-breather; sore throats; poor appetite; fretful.	Moderately enlarged at angle jaw on both sides.	Tonsils: Enlarged. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 99° F. W. B. C.: 13,600. No general glandular enlargement.
L. H. 35949. Female.	W	5	Frequent colds; discharge left ear; mouth-breather.	Enlarged. (Pediculosis capitis.)	Tonsils: Enlarged. Teeth: Carious. Adenoids: Large mass.	Normal. Temperature: 98.5° F. No general glandular enlargement.
E. L. 36094. Male.	W	2	No history sore throats. Enlarged glands neck; mouth-breather. On right glands began to enlarge when child was 2 months of age.	Much enlarged glands angle jaws; very evident on inspection; very suggestive of Tbc. glands.	Tonsils: Meet in mid-line. Adenoids: Very large mass. Teeth: Good.	Normal. Temperature: 98.6° F.
A. W. 36638. Male.	W	5	Enlarged gland angle jaw left for 6 weeks. Mouth-breather; frequent colds.	Measures 3 x 5 cm. angle jaw left; hard; not adherent (diagnosed in Surg. Disp. Tbc. gland.)	Tonsils: Enlarged. Adenoids: Large amount. Teeth: Carious.	X-ray chest normal. Von Pirquet: Negative. R. B. C.: 4,400,000. W. B. C.: 14,000. Hb.: 90%. No general glandular enlargement. Temperature: 98° F.
K. M. 36684. Female.	C	3	Swelling glands neck; difficulty in breathing; discharge from ears; peritonsillar abscess 3 weeks ago.	Enlarged at angle jaw both sides; very evident on inspection. (Noticed for 1 year.)	Tonsils: Enlarged. Teeth: Carious. Adenoids: Large mass. Ears: Drums retracted.	Normal. Temperature: 98.5° F. General glandular enlargement. Pirquet test: Negative.
A. R. 37153. Female.	C	4	Frequent colds and sore throat; swelling glands neck; nasal discharge; mouth breather.	Gland angle left jaw 2 x 2 cm.; hard; movable; enlarged in other triangles.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 99° F. General glandular enlargement.
M. J. 37311. Female.	W	3	Suppurated gland right angle jaw 1 month; discharging; frequent colds; vomiting, fever.	Discharging mass glands angle jaw on right; also enlarged down sternomastoid on right; slightly on left. (Very suggestive Tbc. glands.)	Tonsils: Slightly enlarged; adherent to pillars. Adenoids: Infected; discharge. Teeth: Good.	Normal. Pirquet test: Negative. No general glandular enlargement.
T. H. 37326. Male.	W	4	Chronic cough 6 months; mouth-breather; frequent colds.	Enlarged at angle jaws; slightly enlarged posterior triangles.	Tonsils: Enlarged; adherent. Adenoids: Large mass. Nose: Deflected septum right. Malocclusion.	Normal. Temperature: 99° F. No general glandular enlargement. Pirquet test: Negative.
A. N. 37837. Female.	W	4	Chronic cough; mouth-breather; frequent colds; tonsillitis 4 months ago. Appetite poor.	Enlarged at angle jaws and slightly in posterior triangles.	Tonsils: Very large. Adenoids: Very large. Teeth: Good.	Normal. Temperature: 99.5° F. Pirquet: Negative.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.
I. CASES BETWEEN 1 AND 5 YEARS OF AGE.—Continued.

Date and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
June, 1913. Cervical adenitis. Mouth-breather.	None.	Sept., 1915. Frequent colds and epistaxis; otherwise perfectly well.	Not palpable in anterior triangle on either side; small in posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia in pharynx; otherwise normal. Nose and ears look normal.	Well.
July, 1913. Cervical adenitis. Mouth-breather.	None.	July, 1915. Perfect health; no headaches since operation. Has grown rapidly.	Two or three glands angle jaw right measure $\frac{1}{2}$ cm. diameter; not palpable in anterior triangle left.	Teeth: Good. Throat: Looks normal. Ears: Normal.	Well: Palpable glands remain at angle jaw on right after 2 years.
Oct., 1913. Cervical adenitis (Tbc.?). Mouth-breather.	None.	Sept., 1915. Perfect health; not sick in past 2 years.	On right at angle jaw hard, discrete gland 2 x 1 cm. Not palpable on left.	Teeth: Carious. Throat: Looks normal. Nose and ears: Normal.	Apparently well, although still enlarged gland at angle jaw on right.
Nov., 1913. Cervical adenitis (Tbc.?). Mouth-breather.	None.	Oct., 1915. Is healthy, strong, well grown. No trouble with ears. Breathes normally.	At angle jaw on right about 2 x 1 cm.; hard; movable. Just palpable on left and in posterior triangles.	Teeth: Good. Throat: Looks normal. Nose and ears: Normal.	Apparently well, although still enlarged gland at angle jaw on right.
Nov., 1913. Chronic tonsillitis. Mouth-breather.	None.	Feb., 1916. Just recovered from scarlet fever; general health excellent.	Barely palpable on left; not palpable on right.	Throat: Normal. Nose and ears: Normal.	Well.
Dec., 1913. Cervical adenitis. Chronic bronchitis (?). Mouth-breather.	None.	Feb., 1916. Excellent. No cough; normal weight. Lungs clear on perc. and ausc.	Barely palpable in anterior and posterior triangle on right. Not felt left.	Teeth: Carious, especially right. Throat: Lymphoid hyperplasia; otherwise normal.	Well.
Dec., 1913. Chronic tonsillitis. Cervical adenitis. Mouth-breather.	None.	June, 1915. General health good; only two or three colds in past 2 years.	Not palpable in anterior triangle either side. Just felt on left in posterior triangle.	Teeth: Carious. Throat: Lymphoid hyperplasia; otherwise normal. Ears and nose: Normal.	Well.
Jan., 1914. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Excellent; grown rapidly; good appetite; breathes normally.	Barely palpable in anterior and posterior triangles.	Teeth: Carious. Throat: Normal. Nose and ears: Normal.	Well.
May, 1914. Cervical adenitis (Tbc.?). Mouth-breather.	None.	Mar., 1916. Excellent; not sick since operation.	Barely palpable on right; not felt on left.	Throat: Lymphoid hyperplasia; otherwise normal. Teeth: Carious. Nose and ears: Normal.	Well.
May, 1914. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Perfectly well since operation. Well grown healthy looking child.	Not palpable in anterior triangles on either side; just felt in posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia; otherwise normal. Nose and ears: Normal.	Well.
May, 1914. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Has had no colds or other illness since operation. Still sleeps with mouth open.	Are not palpable in anterior or posterior triangles.	Teeth: Carious upper right; lower left. Throat: Looks normal. Nose and ears: Normal.	Well. Cervical glands not palpable, although teeth are still carious.
June, 1914. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Still has spasmodic choking cough only at night; otherwise good health.	Barely palpable at angle jaws. About size bean in submaxillary triangle on right.	Teeth: Good. Throat: Looks normal with exception lymphoid hyperplasia. Larynx: Normal.	Very slight impairment lower left back; no râles. Von Pirquet: Negative. Abdomen: Normal.
July, 1914. Chronic tonsillitis. Chronic otitis media. Mouth-breather.	None.	June, 1915. No sore throat or trouble with ears since operation. Still sleeps with mouth open. Otherwise in excellent health.	Slightly enlarged submaxillary glands on both sides. Glands at angle jaw not palpable; just palpable in posterior triangles.	Teeth: Carious; abscess lower left. Throat: Lymphoid hyperplasia on pharynx. Ears: Drums retracted but normal. Nose: Normal.	Well. Referred to dental department.
Aug., 1914. Cervical adenitis. Mouth-breather. Otitis media.	None.	June, 1915. General health good; no trouble with ears. Breathing normal.	Barely palpable, discrete glands at angles jaw.	Teeth: Good. Throat: Lymphoid hyperplasia. Nose and ears: Look normal.	Well.
Sept., 1914. Chronic tonsillitis. Mouth-breather. Chronic cough.	None.	Nov., 1915. No colds; cough; breathes normally; has grown rapidly.	Just palpable on right; not felt on left.	Throat: Lymphoid hyperplasia; otherwise normal. Teeth: Good. Nose and ears: Normal.	Well.
Oct., 1914. Chronic tonsillitis. Mouth-breather. Otitis media.	None.	Nov., 1915. "Perfectly well in every way."	Not palpable on left; just felt on right.	Teeth: Carious. Nose and ears: Normal.	Well.
Nov., 1915. Cervical adenitis (Tbc.?). Mouth-breather.	None.	Aug., 1915. Much improved; eats well; sleeps well.	Just palpable on left; measure about 1 x 1 cm. on right.	Throat: Lymphoid hyperplasia. Teeth: Good. Throat: Looks normal.	Well.
Dec., 1915. Cervical adenitis. Mouth-breather.	None.	Nov., 1915. Much improved; no cold since operation. Still sleeps with mouth open.	Gland at angle left jaw about $\frac{1}{2}$ cm. in diameter; just palpable on right.	Teeth: Carious lower left. Throat: Looks normal. Ears: Drums retracted.	Well. Gland disappeared, although carious tooth remains.
Jan., 1915. Cervical adenitis. Chronic tonsillitis.	None.	Nov., 1915. Much improved. Hearing almost normal. Breathing normal.	Glands not palpable in anterior triangle; just felt posterior triangle.	Teeth: Carious lower right and left. Throat: Looks normal. Ears: Drums slightly retracted.	Well. Gland disappeared, although carious tooth remains.
Feb., 1915. Cervical adenitis. Mouth-breather.	None.	Nov., 1915. No colds since operation. Breathes normally.	Glands barely palpable on left; not palpable right in anterior triangle. Small, shot-like in posterior triangle.	Teeth: Good. Throat: Looks normal. Nose and ears: Normal.	Well.
Mar., 1915. Cervical adenitis (Tbc.?). Chronic tonsillitis. Facial curettage infected (and on right.)	None.	Nov., 1915. Much improved. One vomiting attack since operation. No colds.	Scar right; glands at angle jaw and in anterior triangle just palpable on both sides; not palpable in posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia. Nose and ears: Normal.	Well.
Apr., 1915. Chronic tonsillitis. Mouth-breather.	None.	Nov., 1915. No cough since operation. Breathes normally through nose.	Barely palpable in anterior and posterior triangles.	Throat: Lymphoid hyperplasia on pharynx.	Well.
May, 1915. Chronic tonsillitis. Mouth-breather.	None.	Feb., 1916. No cough since operation, but frequent colds. Appetite good.	Barely palpable in anterior and posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia. Ears: Normal.	Well.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT.
II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
M. D. 29215. Female.	W	8	Frequent sore throat. Impaired speech; mouth-breather; adenoid facies.	Enlarged at angle jaw; also sub-maxillary glands.	Tonsils: Meet in mid-line. Adenoids: Large mass. Teeth: Good.	Normal. W. B. C.: 12,200. Hb.: 75%. Temperature: 98.5° F. General glandular enlargement. Poorly nourished; pale. W. B. C.: 11,200. Hb.: 70%. Temperature: 99° F. Bronchial râles. Temperature: 98° F. Otherwise normal.
B. K. 29783. Female.	W	7	Frequent tonsillitis with fever and swelling glands neck; epistaxis; headache; pale; poor appetite.	Enlarged at angles jaw.	Tonsils: Very large. Adenoids: Very large. Teeth: Good.	Normal. W. B. C.: 11,200. Hb.: 70%. Temperature: 99° F. Bronchial râles. Temperature: 98° F. Otherwise normal.
L. E. 30916. Female.	W	6	Swelling glands neck; mouth-breather; occasional tonsillitis; cough.	About size hickory-nuts at each angle jaw; hard.	Tonsils: Almost meet. Adenoids: Very large. Teeth: Carious.	Normal. W. B. C.: 12,200. Hb.: 75%. Temperature: 98.5° F. General glandular enlargement. Poorly nourished; pale. W. B. C.: 11,200. Hb.: 70%. Temperature: 99° F. Bronchial râles. Temperature: 98° F. Otherwise normal.
C. D. 31083. Female.	W	9	Frequent sore throat; mouth-breather.	Enlarged in anterior and posterior triangles.	Tonsils: Enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 98° F.
C. K. 31136. Male.	W	10	Swelling glands left side neck; mouth-breather; frequent colds.	Mass glands angle jaw left size egg; hard; adherent.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Good.	Lungs normal. Temperature: 98.5° F.
A. L. 31219. Female.	W	9	Frequent colds; mouth-breather.	Enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 98.6° F.
F. L. 31220. Female.	W	10	No history sore throat; chronic cold; mouth-breather.	Enlarged especially left (Pediculosis capitis).	Tonsils: Enlarged, especially right. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98.6° F.
E. W. 31607. Female.	C	8	Frequent colds and sore throat; mouth-breather.	Enlarged anterior and posterior triangles.	Tonsils: Enlarged. Adenoids: Enlarged. Ears: Chronic catarrhal otitis media left.	Normal. Temperature: 98.2° F.
J. E. 31632. Female.	W	9	Sore throat frequent for 2 or 3 years; mouth-breather.	Enlarged angle jaws, especially left.	Tonsils: Left larger than right. Adenoids: Large. Teeth: Carious.	Normal. Temperature: 98° F.
T. H. 31789. Male.	W	8	Frequent tonsillitis; constant nasal cold; mouth-breather; enlarged glands.	Enlarged angles jaw both sides.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Good.	Normal. Temperature: 98.6° F.
L. H. 31828. Male.	W	7	No history sore throat; enlarged cervical glands; mouth-breather.	Much enlarged angles jaw.	Tonsils: Much enlarged. Adenoids: Mouth-breather; large. Teeth: Carious.	Normal. Temperature: 98° F.
V. W. 31845. Female.	W	7	Frequent sore throat past 3 years; mouth-breather.	Enlarged on right at angle jaw; just palpable on left.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. W. B. C.: 4800. Hb.: 80%. Temperature: 99° F.
E. B. 31866. Female.	W	8	Frequent tonsillitis for 3 years; mouth-breather; pains knees; earache.	Slightly enlarged angles jaw.	Tonsils: Meet in mid-line. Adenoids: Large mass. Teeth: Carious.	Normal. W. B. C.: 7000. Hb.: 88%. Temperature: 99° F. Diag. pulmonary Tbc. in Phipps Dispensary. Temperature: 99° F.
A. L. 31968. Male.	W	6	Chronic cough; anæmic; enlarged cervical glands; hoarseness; always delicate physically, and mentally retarded; mouth-breather.	Size walnut at angles jaw; matted together (Tbc.?).	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Good. Vocal cords: Red; otherwise normal.	Poorly nourished; otherwise negative. Temperature: 99° F.
M. M. 32025. Female.	W	10	Frequent sore throat; mouth-breather; chronic cough.	Enlarged.	Tonsils: Meeting in mid-line. Adenoids: Large mass. Teeth: Carious.	Systolic murmur apex; not transmitted. Otherwise normal. Temperature: 98.6° F.
M. Z. 32073. Female.	W	10	Frequent sore throat; mouth-breather; chronic cough.	Enlarged in all triangles.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98.6° F.
A. H. 32144. Female.	W	10	Swelling glands neck; frequent sore throat; mouth-breather.	Size walnuts angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 98.6° F.
J. P. 32238. Male.	W	7	Swelling glands neck; frequent sore throat; impaired hearing; epilepsy.	Enlarged angles jaw.	Tonsils: Small; embedded. Adenoids: Small amount. Teeth: Carious; malocclusion. Ears: Chronic catarrhal otitis media.	Normal. Temperature: 98.4° F.
A. S. 32362. Male.	W	6	Mouth-breather.	Size walnut angle jaw left; enlarged in other triangles.	Tonsils: Not enlarged; adherent to pillars. Adenoids: Large. Teeth: Good.	Normal. Temperature: 98.6° F.
N. D. 32381. Female.	W	6	Swelling glands neck; mouth-breather; frequent colds.	Evident on inspection angles jaw both sides.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Good.	Normal. Temperature: 98.8° F.
W. E. 32435. Male.	W	7	Sore throat; mouth-breather; earache.	Enlarged angles jaw.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Good.	Normal. Temperature: 99° F.
G. S. 32666. Female.	W	6	Sore throat; earache; mouth-breather.	Much enlarged on right.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious.	Normal. Temperature: 98.8° F.
M. C. 32752. Female.	W	8	Swelling glands neck; frequent sore throat; mouth-breather.	Evident on inspection angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 99° F.
E. S. 32832. Female.	W	8	Sore throat; earache; mouth-breather.	Much enlarged on left.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 99° F.
L. L. 32835. Female.	W	10	Swelling glands neck; headaches; mouth-breather.	Evident on inspection on both sides at angle jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: No note.	Normal. Temperature: 98.4° F.
J. M. 32724. Female.	W	8	Sent by school inspector; mouth-breather.	Much enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 99.5° F.
R. S. 32780. Female.	W	7	Frequent sore throat; mouth-breather.	Slightly enlarged at angles jaw.	Tonsils: Not enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 98.6° F.
B. S. 32872. Male.	W	8	Swelling glands neck; frequent sore throat; mouth-breather.	Size almonds at angle jaw on each side.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98.6° F.
W. C. 32892. Male.	W	7	Swelling glands neck; frequent tonsillitis; headache.	Size walnuts each side at angle jaw.	Tonsils: Small; imbedded. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 98° F.
J. C. 32891. Male.	W	9	Swelling glands neck; frequent sore throat.	Size walnuts each side at angle jaw.	Tonsils: Small; adherent to pillars. Adenoids: Small; infected. Teeth: No note.	Normal. Temperature: 98° F.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.
II. CASES BETWEEN 6 AND 10 YEARS OF AGE.

Date and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
Feb., 1912. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Good; few colds; speech normal.	Just palpable.	Teeth: Good. Throat: Looks normal.	Well.
May, 1912. Chronic tonsillitis. Mouth-breather.	None.	Aug., 1915. Perfectly well since operation.	About ½ cm. in diameter at angles jaw; others small.	Teeth: Good. Throat: Looks normal.	Well.
Nov., 1912. Chronic tonsillitis. Cervical adenitis.	None.	June, 1915. No sore throat since operation. No headaches.	At angle jaw on right glands about 1 x 1 cm.; discrete; hard. Slightly enlarged in other triangles.	Teeth: Carious. Throat: Lymphoid hyperplasia. Nose and ears: Normal.	Well, although cervical glands still slightly enlarged.
Dec., 1912. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Only one cold since operation.	About size shot in the anterior and posterior triangles.	Teeth: One carious. Throat: Looks normal. Nose and ears: Look normal.	Well.
Dec., 1912. Cervical adenitis. Mouth-breather.	None.	Nov., 1915. Perfectly well; breathes normally.	Not palpable in anterior or posterior triangle either side.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
Dec., 1912. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Perfectly well; breathes normally.	Not palpable in anterior triangles; just palpable posterior triangle.	Teeth: Good. Throat: Looks normal.	Well.
Dec., 1912. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Only one cold since operation.	Barely palpable in anterior and posterior triangles.	Teeth: Carious. Throat: Looks normal.	Well.
Feb., 1913. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Perfectly well.	Still slightly enlarged at angles jaw.	Teeth: Carious. Throat: Lymphoid hyperplasia. Nose: Hypert. inf. turb.	Well.
Mar., 1913. Chronic tonsillitis. Cervical adenitis.	None.	July, 1915. Perfectly well.	Still slightly enlarged in both anterior and posterior triangles.	Teeth: Good. Throat: Looks normal.	Well.
Mar., 1913. Chronic tonsillitis. Mouth-breather.	None.	Nov., 1915. Frequent colds; otherwise good.	Not enlarged; just palpable at angles jaw and posterior triangles.	Teeth: Good. Throat: Looks normal.	Well.
Mar., 1913. Chronic tonsillitis. Cervical adenitis.	None.	June, 1915. Well.	Barely palpable in anterior and posterior triangles.	Teeth: Many carious; alveolar abscess upper right molar. Throat: Looks normal.	Well. Enlarged cervical glands disappeared, although teeth still carious; also alveolar abscess.
April, 1913. Chronic tonsillitis. Cervical adenitis.	None.	June, 1915. Headaches (eyes?); otherwise good.	Not palpable at angles jaw.	Teeth: Good condition. Throat: Lymphoid hyperplasia.	Well.
April, 1913. Chronic tonsillitis. Mouth-breather.	None.	May, 1913. Much improved; no sore throat; joints normal; breathes normally.	Still slightly enlarged at angles jaw and in posterior triangles.	Teeth: Many carious. Throat: No note.	Well.
May, 1913. Cervical adenitis. Mouth-breather.	None.	July, 1915. Much improved; no cough since operation. Still sleeps with mouth open.	One gland angle jaw right ½ cm. diameter; smaller on left.	Teeth: Carious. Throat: Looks normal. Vocal cords: Normal.	Well.
May, 1913. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Perfectly well; healthy looking.	Barely palpable.	Teeth: Carious lower jaws. Throat: Lymphoid hyperplasia.	Well.
May, 1913. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Well.	Angle jaw right barely palpable; not palpable left.	Teeth: Good. Throat: Looks normal.	Well.
May, 1913. Chronic tonsillitis. Cervical adenitis.	None.	June, 1915. Perfectly well except headache.	Not palpable in anterior triangles; just palpable left posterior triangles.	Teeth: Good. Throat: Discharge from nasopharynx. Nose: Antrum infection.	Well.
May, 1913. Chronic tonsillitis.	None.	July, 1915. Treated H. L. H. for epilepsy. No sore throat or cold since operation.	Submaxillary triangles glands enlarged; posterior triangles slightly enlarged.	Teeth: Carious. Throat: Looks normal. Ears: As before.	Epilepsy not improved.
June, 1913. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Well.	Measure 1 x 1 cm. at angles jaw; not palpable posterior triangles.	Teeth: Good. Throat: Looks normal. Nose: Looks normal.	Well. Glands still slightly enlarged.
June, 1913. Cervical adenitis. Mouth-breather.	None.	June, 1915. Perfectly well; grown rapidly.	Small, shotty glands at each angle jaw.	Teeth: Carious; abscess lower molar left. Throat: Looks normal.	Well. Glands decreased in size, although teeth carious and alveolar abscess.
July, 1913. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. No earache; much improved.	Barely palpable.	Teeth: Carious. Throat: Looks normal. Ears: Normal.	Well.
Aug., 1913. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Perfectly well.	Not palpable on either side.	Throat: Looks normal. Ears: Look normal.	Well.
Aug., 1913. Chronic tonsillitis. Mouth-breather.	None.	Aug., 1915. Well.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well.
Sept., 1913. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Well.	Not palpable.	Teeth: Carious. Throat: Looks normal.	Well.
Sept., 1913. Chronic tonsillitis. Cervical adenitis.	Bleeding from nasopharynx controlled with difficulty.	June, 1915. Still mouth-breather; otherwise perfectly well.	Not palpable.	Teeth: Good. Throat: Looks normal. Nose: Deflected septum.	Well.
Sept., 1913. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well.
Sept., 1913. Chronic tonsillitis.	None.	June, 1915. Well.	Barely palpable.	Teeth: Carious; alveolar abscess upper right. Throat: Looks normal.	Well.
Sept., 1913. Cervical adenitis.	None.	June, 1915. Well; gained 15 pounds weight.	Not palpable.	Teeth: Carious. Throat: Looks normal.	Well.
Sept., 1913. Cervical adenitis.	None.	July, 1915. Well.	Small shotty glands in all triangles.	Teeth: Many carious. Throat: Looks normal.	Well.
Sept., 1913. Cervical adenitis.	None.	July, 1915. Well.	Not palpable on right; at angle jaw left measures ½ cm. diameter.	Teeth: One carious left. Throat: Lymphoid hyperplasia.	Well.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT
II CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
A. R. 33051. Female.	W	10	Swelling glands neck; frequent colds; mouth-breather; frequent sore throat.	Enlarged both sides.	Tonsils: Not enlarged. Adenoids: Small; infected. Teeth: Carious.	General glandular enlargement. W. B. C.: 18,700. Hb.: 80%. Temperature: 98.6° F. Normal.
C. G. 33170. Female.	W	9	Frequent colds; chronic cough; mouth-breather.	Slightly enlarged at angle jaws.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Good.	Temperature: 98.6° F. Normal.
R. T. 33214. Male.	W	7	Frequent sore throat; mouth breather.	Enlarged on both sides.	Tonsils: Not enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 98.6° F.
J. P. 33253. Male.	W	7	Frequent sore throat; mouth breather.	Enlarged on both sides.	Tonsils: Meet in mid-line. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 98.4° F.
H. F. 33310. Female.	W	9	Frequent sore throat.	Evident on inspection both sides.	Tonsils: Meet in mid-line. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 99° F.
R. B. 33349. Female.	W	9	Swelling glands neck; infrequent sore throat; mouth-breather.	Size walnuts at both angles of jaw.	Tonsils: Much enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 98.6° F.
E. H. 33357. Male.	W	10	Frequent sore throat; anorexia.	Enlarged both sides.	Tonsils: Large. Adenoids: Small. Teeth: Good.	Normal. Temperature: 99° F.
A. W. 33361. Female.	W	9	Sore throat; mouth-breather.	Enlarged both sides.	Tonsils: Small; imbedded. Adenoids: Small; infected. Teeth: Good.	Normal. Temperature: 98.4° F.
N. C. 33550. Male.	W	7	Sent by school inspector.	Size walnuts both sides at angle jaws.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Many carious.	Normal. Temperature: 98° F.
J. S. 33566. Male.	W	7	Swelling glands neck; mouth-breather.	Enlarged both sides.	Tonsils: Very large. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 98.2° F.
L. N. 33599. Male.	W	7	Swelling glands neck; no history sore throat.	Size walnuts angle jaws.	Tonsils: Very large. Teeth: Good.	Normal. Temperature: 98.4° F.
G. M. 33621. Female.	W	6	Sore throat; mouth-breather.	Enlarged angle jaws.	Adenoids: Large mass. Tonsils: Meet in mid-line. Adenoids: Very large.	Normal. Temperature: 99° F.
E. M. 33622. Female.	W	8	Sore throat; mouth-breather.	Size walnut angle jaw left; hard.	Teeth: Good. Tonsils: Enlarged. Adenoids: Enlarged.	Normal. Temperature: 99.6° F.
J. W. 33689. Male.	W	9	Frequent sore throat for 2 years.	Enlarged both sides.	Teeth: Carious. Tonsils: Meet in mid-line. Adenoids: Large mass.	Normal. Temperature: 100° F.
W. R. 33704. Male.	W	9	Frequent sore throat; mouth-breather.	Enlarged both sides.	Teeth: No note. Tonsils: Meet in mid-line. Adenoids: Very large.	Normal. Hb.: 80%.
L. A. 33759. Female.	W	7	Earache; mouth-breather. History c. s. meningitis, and pneumonia.	Enlarged both sides.	Teeth: No note. Tonsils: No note. Adenoids: Large mass.	Temperature: 99° F. Systolic murmur apex and axilla. Extra systole. Temperature: 98.4° F.
G. B. 33784. Male.	W	9	Mouth-breather for 2 years.	Enlarged both sides.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. W. B. C.: 10,200. Hb.: 73%.
M. H. 33937. Female.	W	6	Sore throat; mouth-breather; earache.	Enlarged both sides.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious.	Temperature: 98.6° F. General glandular enlargement. Systolic murmur apex and axilla. Br. rales over both lungs.
K. G. 34308. Male.	W	9	Swelling angle jaw right 4 months; no history sore throat. (Swelling due to dentigerous cyst.)	Enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Dentig. cyst lower right.	Normal. Temperature: 99° F.
B. Z. 34333. Male.	W	8	Spitting blood.	Much enlarged at angles jaw.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Many carious.	Normal. Temperature: 98° F.
M. McK. 34334. Female.	W	10	Frequent sore throat.	Much enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 99.2° F.
E. B. 34335. Female.	W	10	Frequent sore throat; headache; earache.	Enlarged both sides; about 3 x 4 cm. angle jaw left.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Good.	Normal. Temperature: 98° F.
E. B. 34336. Female.	C	6	Sore throats; mouth-breather.	Enlarged both sides angle jaw.	Ears: Chronic suppurative otitis media. Tonsils: Much enlarged. Adenoids: Much enlarged.	Normal. Temperature: 98.4° F.
H. M. 34490. Female.	C	10	Sore throat; mouth-breather.	Size almond on right; just palpable left angle jaw.	Teeth: Carious. Tonsils: Enlarged. Adenoids: Enlarged.	Normal. Ascariis infection. W. B. C.: 8200.
M. M. 34538. Female.	W	7	Swelling glands neck left; frequent sore throat; mouth-breather.	Size walnut left angle jaw; smaller on right. Hard, discrete.	Hb.: 85%. Temperature: 98.6° F. Normal (lungs O. K.). W. B. C.: 19,000.	Hb.: 65%. Temperature: 99° F. Normal.
R. S. 34783. Female.	W	10	Frequent sore throat.	Enlarged both sides.	Teeth: Carious. Tonsils: Enlarged. Adenoids: Enlarged.	Temperature: 99° F. Normal.
A. H. 34840. Male.	W	8	Sore throat; earache; mouth-breather.	Slightly enlarged both sides.	Teeth: Good. Tonsils: Enlarged. Adenoids: Enlarged.	Normal. Temperature: 99° F.
R. A. 34857. Female.	W	6	Cough; mouth-breather; earache right.	Enlarged both sides.	Teeth: Carious. Tonsils: Enlarged. Adenoids: Enlarged.	Normal. Temperature: 98.8° F.
J. S. 34888. Male.	W	9	Sore throat; mouth-breather.	Enlarged on left 2 x 3 cm.	Teeth: Carious. Tonsils: Enlarged. Adenoids: Enlarged.	Systolic murmur, not transmitted. Normal otherwise.
M. H. 35003. Female.	C	8	Sore throat frequent.	Slightly enlarged.	Teeth: No note. Tonsils: Enlarged. Adenoids: Enlarged.	Normal. Temperature: 98.5° F.
N. S. 35012. Female.	W	6	Earache; sore throat.	Enlarged.	Teeth: Carious. Tonsils: Enlarged, especially left. Adenoids: Enlarged.	Normal. Temperature: 99.2° F.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.
II CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

Date and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
Oct., 1913. Chronic tonsillitis.	None.	July, 1915. Well.	Barely palpable at angles jaw.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
Oct., 1913. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Has had several colds; otherwise well.	Not palpable in anterior triangles; size shot in posterior triangles.	Teeth: Good. Throat: Looks normal.	Well.
Nov., 1913. Chronic tonsillitis. Mouth-breather.	None.	Dec., 1915. Perfectly well; breathes normally.	Not palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
Nov., 1913. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Still quite nervous; otherwise well.	Barely palpable.	Teeth: Carious. Throat: Looks normal.	Well.
Nov., 1913. Chronic tonsillitis.	None.	Feb., 1916. Perfectly well since operation.	Not palpable either side.	Throat: Lymphoid hyperplasia.	Well.
Nov., 1913. Cervical adenitis.	Bleeding from nasopharynx.	Aug., 1915. Frequent colds, but no swelling glands neck.	Just palpable on right; not on left.	Teeth: Carious. Throat: Some discharge from nasopharynx.	Well. Glands disappeared, although teeth still carious.
Nov., 1913. Chronic tonsillitis.	None.	Oct., 1915. Perfectly well.	Size bean angle jaw right; not palpable left.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
Nov., 1913. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Palpable left; not palpable right.	Teeth: Carious; malocclusion. Throat: Looks normal.	Well.
Dec, 1913. Cervical adenitis.	None.	July, 1915. Well since operation.	Glands at angle jaws about ½ cm. diameter; numerous small glands posterior triangles.	Nose: Deflected septum left. Teeth: Carious. Throat: Looks normal.	Well.
Dec, 1913. Cervical adenitis.	None.	July, 1915. Perfectly well.	About ½ cm. diameter at angle jaws.	Teeth: Carious lower left. Throat: Lymphoid hyperplasia.	Well.
Jan., 1914. Cervical adenitis.	None.	June, 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Normal.	Well.
Jan., 1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well; grown rapidly.	Barely palpable.	Teeth: Carious lower right. Throat: Looks normal.	Well.
Jan., 1914. Cervical adenitis.	None.	June, 1915. Perfectly well.	Just palpable at angle jaw both sides.	Teeth: Good. Throat: Looks normal.	Well.
Jan., 1914. Chronic tonsillitis.	None.	Oct., 1915. Well.	Size pea at angle jaw right; others not palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
Jan., 1914. Chronic tonsillitis.	None.	June, 1915. Well.	Barely palpable on both sides.	Nose: Hypert. inf. turb. double. Teeth: Carious upper molar. Throat: Lymphoid hyperplasia. Ear: Discharge on right, acute.	Well.
Jan., 1914. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Still discharge from ear; otherwise well.	On left at angle jaw glands 1 cm. diameter; not palpable right. Small, shotty in posterior triangles.	Teeth: Carious. Throat: Discharge from nasopharynx. Ears: Chronic suppurative otitis media double.	Well. Chronic otitis media persists.
Jan., 1914. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Perfectly well.	Barely palpable.	Teeth: Good; malocclusion. Throat: Lymphoid hyperplasia.	Well.
Feb., 1914. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Perfectly well.	Measure 1 x 1 cm. angles jaw both sides; discrete; movable.	Teeth: Many carious. Throat: Looks normal.	Well, although glands still enlarged.
April, 1914. Chronic tonsillitis. Mouth-breather. (Removal dentigerous cyst.)	None.	July, 1915. Perfectly well.	Not palpable.	Teeth: Carious. Throat: Looks normal.	Well.
April, 1914. Chronic tonsillitis.	None.	Jan., 1916. Perfectly well.	Barely palpable each side.	Teeth: One carious. Throat: Looks normal.	Well.
April, 1914. Chronic tonsillitis.	None.	Sept., 1915. Glands occasionally enlarged; headache.	About 1 cm. diameter angles jaw; slightly smaller posterior triangle.	Teeth: Two carious. Throat: Lymphoid hyperplasia.	Improved. Glands neck still enlarged.
April, 1914. Cervical adenitis.	None.	Oct., 1915. No headaches; frequent colds; otherwise well.	1 x 1 cm. at angles jaw both sides; discrete; movable; hard.	Teeth: Good. Throat: Lymphoid hyperplasia. Ears: No discharge; drums retracted; hearing good left, impaired right.	Well.
April, 1914. Chronic tonsillitis.	None.	July, 1915. Perfectly well.	Not palpable on either side.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
May, 1914. Chronic tonsillitis.	None.	Jan., 1916. Perfectly well.	Angle jaw right gland 1 x 2 cm.; smaller left.	Nose: Obstr. rt. hypert. inf. turb. Teeth: Good. Throat: Lymphoid hyperplasia.	Well, although glands still slightly enlarged.
May, 1914. Cervical adenitis.	None.	June, 1915. Nervous; otherwise well.	Enlarged; matted together, typical tbc. glands.	Teeth: Good. Throat: Lymphoid hyperplasia.	Not improved. Tbc. glands neck: microscopic examination tonsils and adenoids shows no Tbc.
June, 1914. Chronic tonsillitis.	None.	July, 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
June, 1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Barely palpable.	Teeth: Carious. Throat: Lymphoid hyperplasia.	Well.
June, 1914. Chronic tonsillitis.	None.	July, 1915. Perfectly well; grown rapidly.	About ½ cm. diameter.	Nose: Deflected septum left. Teeth: Carious upper. Throat: Looks normal. Ears: Normal.	Well.
July, 1914. Cervical adenitis.	None.	June, 1915. Well.	Not palpable.	Teeth: Carious. Throat: Lymphoid hyperplasia.	Well.
July, 1914. Chronic tonsillitis.	None.	Nov., 1915. Well.	Not palpable.	Teeth: Carious. Throat: Lymphoid hyperplasia.	Well.
July, 1914. Chronic tonsillitis.	None.	June, 1915. Well.	Not palpable.	Teeth: Good. Throat: Discharge from nasopharynx. Nose: Discharge left side.	Well.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT.
II. CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

Name, Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
I. G. 35085. Female.	C	9	Headache; frequent tonsillitis; mouth-breather; nosebleeds.	Size walnut angle jaw left.	Tonsils: Small, adherent to pillars. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 99° F.
C. W. 35227. Male.	C	6	Impaired speech; frequent sore throat; mouth-breather.	Enlarged.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Carious.	Normal. Temperature: 98.6° F.
D. S. 35239. Female.	W	7	Frequent sore throat; mouth-breather; earache; nosebleed q. n.	Much enlarged both sides.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Uncle died this hospital with hemophilia. Normal. Temperature: 98.6° F.
E. H. 35268. Female.	W	9	Frequent tonsillitis and nosebleed.	Size hickory nut left angle jaw.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Carious.	Normal. Temperature: 98.4° F.
A. Q. 35319. Male.	W	6	Enlarged glands since septic pharyngitis (milk) in 1912.	Size walnut on each side angle jaw.	Tonsils: Densely adherent; small. Adenoids: Very large. Teeth: Good.	Normal. Temperature: 99.8° F.
H. S. 35394. Male.	W	8	Sore throat; mouth-breather.	Enlarged.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 98° F.
I. S. 36654. Male.	W	7	Diagnosis Phipps Dispensary: Cervical ad. Tbc. No history sore throat.	Mass glands each angle jaw about 3 x 5 cm.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal (lungs). Temperature: 98.5° F.
A. B. 36640. Female.	C	10	Swelling glands neck. Frequent tonsillitis.	Evident on inspection each angle jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal (lungs). Temperature: 99° F.

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

M. S. 30705. Female.	W	12	Mouth-breather; chronic nasal cold.	Enlarged.	Tonsils: Not enlarged; imbedded. Adenoids: Large mass. Teeth: Carious.	General glandular enlargement. W. B. C.: 10,700. Hb.: 80%. Temperature: 98.4° F.
E. R. 30858. Female.	C	13	Chronic sore throat.	Enlarged both sides.	Tonsils: Much enlarged. Adenoids: Small amount. Teeth: Carious.	Normal. Temperature: 98.6° F.
H. M. 31098. Male.	W	14	Frequent sore throat; mouth-breather. Adenoid facies.	Evident on inspection angle jaws.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: No note.	Normal. W. B. C.: 7600. Hb.: 70%. Temperature: 98° F.
C. H. 31157. Female.	W	12	Frequent sore throat; chronic laryngitis; frequent headache, frontal.	Enlarged.	Tonsils: Enlarged. Adenoids: Large mass. Teeth: No note.	Normal. Temperature: 99° F.
V. S. 31231. Female.	W	12	Swelling gland neck; frequent sore throat; loss appetite.	Evident on inspection angle jaws.	Tonsils: Much enlarged; especially left. Adenoids: Much enlarged. Teeth: Good.	Normal. Temperature: 98.6° F.
P. S. 31233. Female.	W	11	Frequent sore throat; general malaise.	Enlarged.	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: Good.	Normal. W. B. C.: 10,500. Hb.: 80%. Temperature: 99° F.
J. C. 31353. Male.	C	12	Swelling glands neck; frequent sore throat.	Evident on inspection angle jaws.	Tonsils: Meet in mid-line. Adenoids: Large mass. Teeth: Good.	Normal. Temperature: 99.2° F.
B. G. 31936. Female.	W	15	Frequent tonsillitis; quinsy; mouth-breather.	Enlarged.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 98.6° F.
W. W. 32050. Male.	W	11	Frequent sore throat; mouth-breather.	Enlarged anterior and posterior triangles.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Temperature: 99° F.
M. B. 32188. Female.	W	13	Frequent tonsillitis for past 3 years.	Evident on inspection angle jaw right; enlarged other triangles.	Tonsils: Very large. Adenoids: Very large. Teeth: Carious.	Normal. W. B. C.: 14,200. Hb.: 98%. Temperature: 99° F.
L. K. 32206. Female.	W	12	Frequent tonsillitis; earache.	Enlarged at angles jaw.	Tonsils: Small; embedded. Adenoids: Small. Teeth: Good.	Normal. Temperature: 99.6° F.
H. H. 32378. Male.	W	11	Frequent tonsillitis; mouth-breather.	Enlarged.	Tonsils: Not enlarged. Adenoids: Enlarged. Teeth: No note.	Trace albumin; no casts; otherwise normal. Temperature: 98.6° F.
E. J. 32539. Male.	W	13	Frequent tonsillitis; mouth-breather.	Enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 99.6° F.
B. G. 33430. Male.	W	14	Frequent tonsillitis for past 2 years.	Size walnut angle jaw right.	Tonsils: Enlarged. Adenoids: Small amount. Teeth: Good.	Normal. Temperature: 98° F.
R. L. 33736. Male.	W	15	Swelling gland neck left; mouth-breather; impaired hearing.	Evident on inspection angle jaw left; palpable on right.	Tonsils: Small; embedded. Adenoids: Small; infected. Teeth: Carious.	Normal. W. B. C.: 6600. Hb.: 95%. Ears: Chronic catarrhal otitis media. Temperature: 99.2° F.
J. C. 33773. Male.	W	12	Frequent tonsillitis for past 2 years; mouth-breather.	Enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98.6° F.
M. F. 33983. Female.	W	12	Frequent tonsillitis; earache.	Size hickory nut angle jaw on right.	Tonsils: Small; embedded. Adenoids: Small. Teeth: Good.	Normal. Temperature: 98.6° F.
C. B. 34013. Male.	W	15	Mouth-breather; occasional sore throat.	Enlarged both sides at angle jaw.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 98° F.
E. J. 34493. Female.	C	13	Frequent tonsillitis.	Enlarged both sides at angle jaw.	Tonsils: Meet in mid-line. Adenoids: Enlarged. Teeth: Carious.	Normal. Temperature: 99.2° F.
J. K. 34916. Male.	W	11	Chronic cough; mouth-breather; sore throat frequent.	Evident on inspection at angle jaw right.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious.	Normal. Temperature: 98.3° F.
M. S. 35023. Female.	W	12	Frequent sore throat; earache.	Enlarged both sides.	Tonsils: Enlarged. Adenoids: Small; infected. Teeth: Carious. Nose: Hypert. inf. turb. right.	Systolic murmur not transmitted; otherwise normal. Temperature: 99.8° F.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.
II. CASES BETWEEN 6 AND 10 YEARS OF AGE.—Continued.

Case and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
1914. Cervical adenitis.	None.	Aug., 1915. Headaches frequent; otherwise well.	½ cm. diameter at each angle jaw.	Teeth: Good. Throat: Looks normal.	Well.
1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well; speech normal.	Barely palpable.	Teeth: Alveolar abscess; carious. Throat: Lymphoid hyperplasia.	Well.
1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Barely palpable.	Teeth: Carious. Throat: Looks normal. Ears: Normal.	Well.
1914. Cervical adenitis.	None.	June, 1915. Well; no nosebleed since operation.	Enlarged on left.	Teeth: Carious right and left.	Well, although glandular enlargement left persists.
1914. Cervical adenitis.	None.	June, 1915. Well.	Barely palpable each side.	Teeth: Good. Throat: Looks normal.	Well.
1914. Chronic tonsillitis.	None.	Sept., 1915. Well.	Not palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1915. Cervical adenitis. (See p. 7).	None.	Nov., 1915. General health good.	1½ x ½ cm. at each angle jaw; movable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Improved.
1915. Cervical adenitis.	None.	Nov., 1915. Well; no colds since operation.	Not palpable.	Teeth: Carious. Throat: Lymphoid hyperplasia.	Well.

III. CASES BETWEEN 11 AND 15 YEARS OF AGE.

1912. Mouth-breather. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well.
1912. Chronic tonsillitis. Cervical adenitis.	None.	Nov., 1915. Perfectly well.	Not palpable.	Teeth: Carious. Throat: Looks normal.	Well. Glandular enlargement disappeared, although teeth still carious.
1912. Cervical adenitis. Mouth-breather.	None.	June, 1915. Perfectly well.	Barely palpable both sides.	Teeth: Gingivitis. Throat: Looks normal.	Well.
1912. Chronic tonsillitis. Mouth-breather.	None.	June, 1915. Well; no headaches; infrequent colds.	Not palpable anterior triangles; just felt left posterior triangle.	Teeth: Carious lower left. Throat: Looks normal.	Well.
1913. Cervical adenitis.	None.	Sept., 1915. Perfectly well.	Not palpable angle jaws; size shot in posterior triangles.	Teeth: Good. Throat: Looks normal.	Well.
1913. Chronic tonsillitis.	None.	Aug., 1915. Perfectly well.	Not palpable angles jaw; just felt in posterior triangles left.	Teeth: Good. Throat: Looks normal.	Well.
1913. Cervical adenitis.	None.	July, 1915. Perfectly well.	Size shot in anterior triangles; slightly enlarged posterior triangles; especially right.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1913. Chronic tonsillitis.	None.	June, 1915. Well; gained 34 pounds since operation.	Not palpable in anterior or posterior triangles.	Throat: Looks normal.	Well.
1913. Chronic tonsillitis.	None.	Jan., 1916. Perfectly well.	Just palpable angles jaw; not palpable posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1913. Cervical adenitis.	None.	Nov., 1915. Perfectly well.	Not palpable.	No note.	Well.
1913. Chronic tonsillitis.	Bleeding due to slipped ligature; vessel caught and ligated.	June, 1915. Perfectly well; gained 39 pounds in weight.	Not palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1913. Chronic tonsillitis.	None.	July, 1915. Perfectly well.	Slightly enlarged both sides.	Teeth: Carious lower jaws. Throat: Lymphoid hyperplasia.	Well.
1913. Chronic tonsillitis.	None.	Sept., 1915. Still mouth-breather; otherwise well.	Size shot in both anterior and posterior triangles.	Teeth: Carious. Throat: Looks normal.	Well.
1913. Chronic tonsillitis.	None.	Oct., 1915. Perfectly well.	Just palpable right; not palpable on left.	Throat: Looks normal.	Well.
1914. Cervical adenitis.	None.	June, 1915. Well, aside from impaired hearing on right.	Not palpable either side.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1914. Chronic tonsillitis.	None.	Oct., 1915. Perfectly well.	Not palpable either side in anterior or posterior triangles.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well.
1914. Chronic tonsillitis. Cervical adenitis.	None.	Sept., 1915. Well. No trouble with ears since operation.	Barely palpable both sides.	Teeth: Good. Throat: Looks normal. Ears: Drums normal.	Well.
1914. Chronic tonsillitis. Mouth-breather.	None.	July, 1915. Perfectly well.	Barely palpable both sides.	Teeth: Good. Throat: Looks normal.	Well.
1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Not palpable anterior or posterior triangle either side. One palpable gland in submaxillary triangle left.	Teeth: Alveolar abscess left lower. Throat: Looks normal.	Well.
1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Just palpable right; not felt on left.	Teeth: Carious upper. Throat: Lymphoid hyperplasia.	Well.
1914. Chronic tonsillitis.	None.	June, 1915. Perfectly well.	Measures 1 x 1 cm. at angles jaw and in posterior triangle.	Teeth: Carious. Throat: Lymphoid hyperplasia. Nose: Hypert. inf. turb. rt.; otherwise normal.	Improved, still some enlargement of cervical glands.

TABLE VIII.—SUMMARY OF 142 CASES IN WHICH THE TONSILS AND ADENOIDS WERE REMOVED ON ACCOUNT OF ENLARGEMENT.
III. CASES BETWEEN 11 AND 15 YEARS OF AGE.—Continued.

Name. Surg. No. Sex.	Race.	Age.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
E. B. 35083. Female.	W	14	Frequent tonsillitis for past 8 years.	Evident on inspection at angle jaw right.	Tonsils: Small; imbedded. Adenoids: Small; infected. Teeth: Good.	Normal. Temperature: 98.6° F.
D. R. 35124. Female.	W	12	Chronic "cold" for 7 years; mentally deficient.	Evident on inspection at angles jaw both sides.	Tonsils: Small; imbedded. Adenoids: Small; infected. Teeth: Carious. Nose: Deflected septum left.	Tr. albumin and few casts; otherwise normal. Temperature: 98.8° F.
G. B. 35187. Female.	W	12	Mouth-breather.	Enlarged both sides.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: No note.	Normal. Temperature: 98.6° F.
B. R. 35426. Female.	C	11	Frequent sore throat; mouth-breather.	Evident on inspection at angles jaw both sides.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious.	Normal. Temperature: 99° F.
D. G. 35440. Female.	W	11	Frequent tonsillitis; earache. Had 3 or 4 tonsil operations.	Evident on inspection at angle jaw left.	Tonsils: Several operations for removal. Adenoids: Small; infected. Teeth: Carious. Ears: Acute otitis media.	Acute double otitis media; otherwise normal. Temperature: 100° F.

IV. CASES OVER 15 YEARS OF AGE.

Name. Surg. No. Sex.	Race.	Age.	Occupation.	Complaint.	Cervical Glands.	Special Examination.	General Physical Examination.
H. G. 29292. Male.	W	24	Student.	Frequent tonsillitis; swelling glands neck; discharge in throat.	Enlarged; hard at angles jaw.	Tonsils: Enlarged; adherent to pillars. Adenoids: Small; infected. Teeth: Good.	Normal. Temperature: 98.7° F.
W. H. 30780. Male.	W	16	Factory.	Frequent tonsillitis for past 2 years; discharge in throat.	Evident on inspection at angles jaw both sides; tendency to mat together (Tbc.?).	Tonsils: Meet in mid-line. Adenoids: Very large. Teeth: No note.	Lungs: Clear on perc. and auscultation. Persistent thymus. W. B. C.: 7000. Hb.: 80%. Temperature: 98.4° F.
E. B. 31203. Male.	C	16	School.	Frequent tonsillitis; headache.	Enlarged both sides.	Tonsils: Enlarged. Adenoids: Small. Teeth: No note.	Normal. Temperature: 98° F.
A. L. 31624. Female.	C	24	Cook.	Swelling glands neck; frequent sore throat; earache. Glands neck enlarged for 1 year.	Large mass glands at angle jaw left; matted together; hard. Measure 4 x 5 cm.	Tonsils: Much enlarged. Adenoids: Much enlarged. Teeth: Carious.	Lungs: Clear on posterior and anterior. Wassermann: Negative. Temperature: 98.4° F.
M. McG. 36433. Female.	W	17	Clerk.	Tbc. glands neck. Diagnosis made in Phipps Dispensary.	Much enlarged in anterior and posterior triangles both sides. (Pediculi in head.)	Tonsils: Small; imbedded. Adenoids: Large mass. Teeth: Carious.	No active Tbc. lesion in lungs; otherwise normal. Temperature: 99° F. Pirquet: Positive.
F. H. 31675. Female.	C	17	Maid.	Chronic sore throat; frequent attacks acute tonsillitis.	Enlarged both sides at angles jaw; hard; movable.	Tonsils: Small; adherent to pillars. Adenoids: Small. Teeth: Good.	Normal. Wassermann: Negative. Temperature: 99° F.
A. J. 32723. Female.	W	18	Clerk.	Frequent sore throat; chronic catarrhal otitis media.	Enlarged both sides at angle jaw.	Tonsils: Much enlarged. Adenoids: Small. Teeth: Good.	Normal. Temperature: 98.6° F.
L. K. 33089. Female.	W	18	Factory.	Frequent tonsillitis. Has had two operations for removal tonsils.	Enlarged both sides at angles jaw.	Tonsils: Enlarged; adherent. Adenoids: Small; infected. Teeth: Carious.	Normal. W. B. C.: 8400. Hb.: 85%. Temperature: 99.2° F.
M. G. 34171. Female.	C	19	Maid.	Frequent tonsillitis; swelling glands neck.	Enlarged at angles jaw on both sides.	Tonsils: Imbedded; adherent. Adenoids: Large mass. Teeth: Carious.	Normal. Temperature: 99.8° F.
A. S. 34782. Female.	W	18		Frequent tonsillitis.	Enlarged at angles jaw.	Tonsils: Enlarged. Adenoids: Large mass. Teeth: Carious.	Normal.
M. P. 34976. Female.	W	20	Clerk.	Swelling glands neck left and frequent tonsillitis.	Size walnut angle jaw on left.	Tonsils: Small; imbedded. Adenoids: Small. Teeth: No note.	Normal.
H. N. 35082. Female.	W	21		Frequent tonsillitis.	Enlarged both sides.	Tonsils: Small; imbedded. Adenoids: Small; infected. Teeth: No note.	Normal.
M. A. 35574. Male.	W	16	Clerk.	Frequent tonsillitis.	Slightly enlarged at angles jaw.	Tonsils: Enlarged; especially right. Adenoids: Large mass. Teeth: No note.	Systolic blow apex not transmitted. R. B. C.: 4,000,000. W. B. C.: 15,500. Hb.: 70%. Temperature: 98.6° F.
T. W. 35937. Female.	W	25	Student.	Frequent tonsillitis; earache.	Size hickory nut angle jaw on left.	Tonsils: Partially removed. Adenoids: Small; infected. Ears: Drums intact.	Normal. Temperature: 98.4° F.
J. S. 37930. Male.	W	21	Orderly.	Frequent tonsillitis.	Enlarged at angles jaw.	Tonsils: Small; adherent. Adenoids: Small. Teeth: Good.	Slight impairment percussion above right clavicle; otherwise normal. Temperature: 98° F.
J. Y. 37995. Female.	W	18		Frequent sore throat and enlarged glands neck since diphtheria.	Size walnut angles jaw both sides; hard; discrete; movable.	Tonsils: Enlarged. Adenoids: Enlarged. Teeth: Good.	Normal. Has lost 22 pounds in weight. Temperature: 99° F.

CERVICAL GLANDS, WITH SUBSEQUENT REPORT ON THEIR CONDITION AFTER DISCHARGE FROM HOSPITAL.—Continued.
III. CASES BETWEEN 11 AND 15 YEARS OF AGE.—Continued.

and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
, 1914. Chronic tonsillitis.	None.	Dec., 1915. Perfectly well; two "colds" since operation.	Slightly enlarged angle jaw right; and in posterior triangle right.	Teeth: Good. Throat: Looks normal.	Well. Glands still slightly enlarged on right side neck.
, 1914. Cervical adenitis.	None.	July, 1915. No nasal discharge since operation.	Slightly enlarged in submaxillary, anterior and posterior triangles.	Teeth: Good. Throat: Looks normal.	Improved. Still some enlargement of cervical glands.
, 1914. Cervical adenitis.	None.	Dec., 1915. Perfectly well.	Just palpable.	Throat: Looks normal.	Well.
, 1914. Cervical adenitis.	None.	July, 1915. Well, aside from headaches. (Referred ophthalmology.)	About ½ cm. in diameter at angles jaw and posterior triangle.	Teeth: Good. Throat: Looks normal.	Well.
, 1914. Cervical adenitis. (aracentesis.)	None.	Feb., 1916. Perfectly well.	Barely palpable.	Teeth: Good. Throat: Looks normal. Ears: Normal.	Well.

IV. CASES OVER 15 YEARS OF AGE.

and Indication for Operation (Tonsillectomy).	Post-operative Complications.	Subsequent Examination.			
		General Health.	Cervical Glands.	Condition of Nose, Throat and Teeth.	Result.
, 1912. Chronic tonsillitis.	None.	July, 1915. Perfectly well; "colds" less frequent since operation.	Not palpable.	No note.	Well.
, 1912. Cervical adenitis.	None.	July, 1915. Perfectly well since operation.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well. (Tbc. skin test.)
, 1912. Chronic tonsillitis.	None.	Sept., 1915. Perfectly well.	Not palpable.	Teeth: Carious lower molar. Throat: Looks normal.	Well.
, 1913. Cervical adenitis. (extraction carious teeth.)	None.	July, 1915. Perfectly well since operation.	Barely palpable.	Teeth: Good. Throat: Looks normal.	Well. (The mic. sections of tonsils and adenoids were lost; may have been tbc.)
, 1915. Cervical adenitis.	None.	Oct., 1915. Improved.	Angle jaw right 1 x 2 cm. Submaxillary triangle left 2 x 4 cm. hard; movable.	Teeth: Alveolar abscess lower left. Throat: Lymphoid hyperplasia. Sinuses: Infection right antrum.	Improved. (This case included in the group of tbc. adenitis without mic. Tbc. in tonsils or adenoids.) (Infect. right antrum.)
, 1913. Chronic tonsillitis. Cervical adenitis.	None.	June, 1915. Well since operation.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well.
, 1913. Chronic tonsillitis.	None.	Nov., 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Looks normal. Ears: Calcium deposit in drums; hearing good.	Well.
, 1913. Chronic tonsillitis.	None.	Sept., 1915. Perfectly well.	Not palpable.	Teeth: Good. Throat: Looks normal.	Well. (Has had two previous operations for removal tonsils.)
, 1914. Chronic tonsillitis.	None.	Oct., 1915. Perfectly well.	Barely palpable.	Teeth: Good. Throat: Lymphoid hyperplasia.	Well. (Has had four previous operations for removal tonsils.)
, 1914. Chronic tonsillitis.	None.	July, 1915. Much improved.	A gland 1 cm. diameter at angle jaw on right; not palpable on left.	Teeth: Carious upper left.	Well.
, 1914. Cervical adenitis.	None.	June, 1915. Perfectly well.	Not palpable.	Throat: Lymphoid hyperplasia.	Well.
, 1914. Chronic tonsillitis.	None.	Oct., 1915. Has lost weight since operation; otherwise good.	Not palpable.	Throat: Lymphoid hyperplasia.	
, 1914. Chronic tonsillitis.	None.	July, 1915. Perfectly well.	Measure about ½ cm. diameter at angle jaws.	Teeth: Carious. Throat: Looks normal.	Well.
, 1914. Cervical adenitis.	None.	July, 1915. Has had several pharyngitis attacks; otherwise good.	Glands slightly larger than at time of operation.	No note.	Not improved.
, 1915. Chronic tonsillitis.	None.	Feb., 1916. Perfectly well.	Not palpable.	Teeth: Good. Throat: Normal.	Well.
, 1915. Cervical adenitis.	None.	Mar., 1916. Has gained 20 pounds since operation; still nervous; eyes prominent; Graefe positive.	Not palpable.	Throat: Lymphoid hyperplasia.	Well.

A LEGEND OF SALERNO.

HOW CONSTANTINE THE AFRICAN BROUGHT THE ART OF MEDICINE TO THE CHRISTIANS.

By CHARLES SINGER, Oxford, England.

I. INTRODUCTION.

Away back in the mists which enshroud the dawn of European medicine stands the shadowy figure of Constantine the African. The only certain facts concerning his history are that he died about 1087, and that in the latter part of the eleventh century works emanating from the school of Salerno were already borrowing from writings to which his name is attached. These writings of Constantine were no original productions. They were, for the most part, mere translations, very badly rendered, from the Arabic of the Egyptian Israelite, Abu Jakub Ishak ben Soleiman el Israeli, known to mediæval medicine as Isaac Judæus (died A. D. 932 or 941). The works of Isaac, though greatly regarded in mediæval times, are themselves in the main little more than versions of various works of Galen. Both Isaac and Constantine derive their main importance in the history of European medicine from the fact that they were the earliest vehicles for the conveyance of the Arabian medical systems to the West.

Practically the only account that we have of the life of Constantine is contaminated from its very source. It is from the hand of Peter the Deacon (1107-1140), librarian of that Monastery of Monte Cassino where most of Constantine's work of translation is said to have been performed. Peter the Deacon is, however, a writer who shows himself credulous and gullible to the last degree. No story is too absurd for him to record, no anachronism too glaring to deter his pen. Furthermore, his main interest in writing is the exaltation of the monastery to which he was attached. Modern research has convicted him of the forgery of documents and the falsification of records. Yet it is on Peter, and Peter only, that we have to rely for the following account of the life of Constantine, which bears on the face of it a legendary character:¹

Constantine the African was a monk of this house (Monte Cassino) and was deeply learned in philosophical studies, both Oriental and Occidental, and was a very Hippocrates for brilliance. Leaving Carthage, where he was born, he went to Babylon, where he fully acquired grammar, dialectic, physic, geometry, arithmetic, mathematics, astronomy, necromancy and music, and he thoroughly learned, moreover, the physic of the Chaldæans, Arabs, Persians and Saracens.

From Babylon he went to India and there he applied himself to the studies of that country. Having completely mastered the arts of the Indians he proceeded to Ethiopia and acquired the discipline of the Ethiopians also. And when he was thus sated with knowledge he went to Egypt and became instructed in all the wisdom of the Egyptians.

¹ For the falsifications of the Monte Cassino MSS. by Peter the Deacon see Erich Caspar "*Petrus Diaconus und die Monte Cassineser Fälschungen. Ein Beitrag zur Geschichte des italienischen Geisteslebens im Mittelalter.*" Berlin, 1909; and E. A. Loew, "*The Beneventan Script,*" Oxford, 1914.

After he had spent nine and thirty years in study, he came again to Carthage [Africa]. But when the people there saw that he was thus filled with the cunning of all the Gentiles, they sought to kill him. Wherefore Constantine secretly took ship and escaped to Salerno and there lay hid for a while disguised as a beggar, till he was recognized by the brother of the king of the Babylonians, who happened to visit there, and so he was hailed in great honor to the house of Duke Robert.

Leaving Salerno, Constantine went to the Monastery of Monte Cassino, and here he was received in all good will by the Abbot Desiderius, and he became a monk. In that very monastery he translated from divers foreign tongues a perfect multitude of works, among which the most important are the following:

The Pantegni, which is divided into twelve books, wherein is set forth what it is meet a physician should know.

The Practica, wherein is laid down how a physician should preserve health and cure disease. It is divided into twelve books.

The Book of twelve Steps (Liber duodecim graduum).

On Food and Diets.

The Book of Fevers, which he rendered from the Arabic.

On the Internal Members.

On Coitus.

The Viaticum, which he divided into seven parts. The first on diseases of the face. Concerning instruments. On diseases of the stomach and intestines. On diseases of the liver, kidneys, bladder, spleen and gall-bladder. On conditions arising in the organs of generation. On all conditions arising in the outer skin [being a work] expounding in sentences the Book of Aphorisms, the Tegni, the Megatechni, the Microtechni, the Antidotarium and the disputations of Plato and Hippocrates.

On Medication with Simples.

The Gynæcia, that is, on the female organs and parts.

On the Pulse.

The Prognostics.

On Experience [De Experimentis].

Glossaries of Herbs and Spices (?) [Specierum].

The Surgery.

The Book of Treatment of the Eyes.

This man spent forty years in acquiring the learning of the nations and he died full of years at Monte Cassino. He was contemporary with the emperors Michael, Constantine, Alexius, and Henricus IV.

Atto, the pupil of Constantine the African and chaplain to the Empress Agnes, copied into elegant Latin style the works which the said Constantine had translated. Atto, Haito or Hetto, for the name is thus variously written, flourished *anno* 1170.¹

This legendary account of Constantine presents numerous difficulties and improbabilities and need hardly be discussed seriously. Even the list of his works, which presumably were

¹ The account here translated occurs in two works of Peter the Deacon:

(a) *De viris illustribus cassinensibus*, Ch. XXIII and XXIV, reprinted in Johan Albert Fabricius, *Bibliotheca Ecclesiastica*, Hamburg, 1718, pp. 180 and 182.

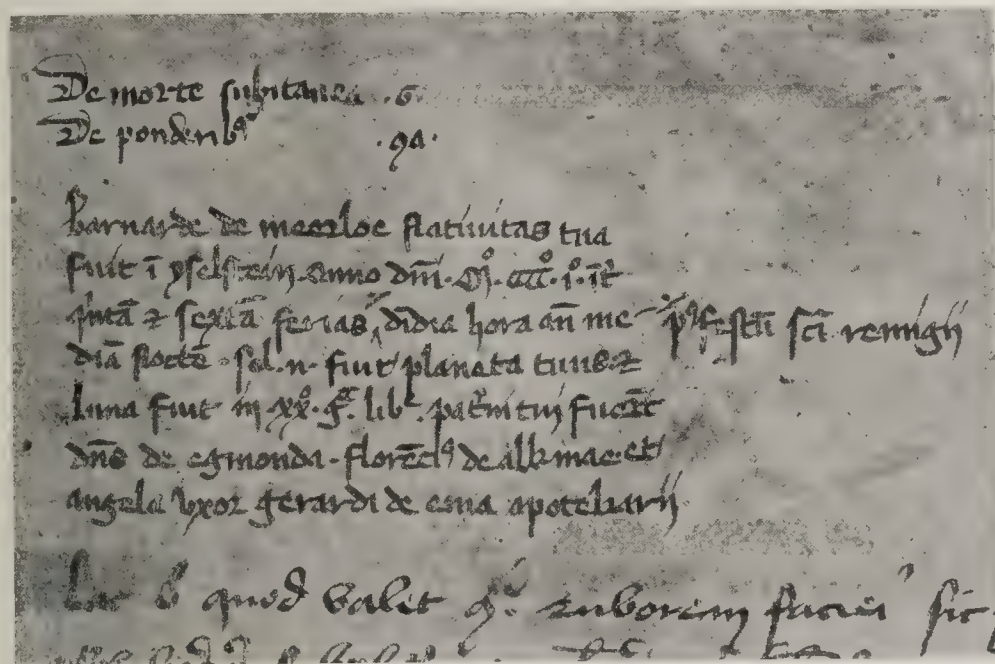
(b) *Chronica monasterii Cassinensis*, Lib. III, Ch. 35, of Leo Mariscanus, bishop of Ostia, continued from the middle of Book III by Peter the Deacon and reprinted in Migne's *Patrologia Latina*, Vol. 173, p. 767, where some minor textual variations are recorded.

before the librarian at Monte Cassino, can hardly be made to fit in with those writings of Constantine that have come down to us. It is, however, possible that an investigation of the surviving manuscripts of Constantine's work might clear up some of the discrepancies. The number, the wide distribution, and the extensive variations in these manuscripts, as well as the frequency with which his writings are quoted, all testify to the great weight attached to his works in mediæval times.

Only one event remains to be added to the account of him given by Peter. There is a tradition that Constantine, before entering the monastery of Monte Cassino, acted as secretary to the Norman Duke, Robert Guiscard, at Salerno, to whom

interesting feature is the rational and scientific spirit in which it is written. The first 62 folios are devoted to the subject of anatomy and form an independent treatise on that subject which it is hoped to publish. Our legend is related in the ordinary course of an anatomical description, and we present it to the reader in this setting.

It is possible to date our manuscript and to fix its provenance within narrow limits. At the very end of the book, after the explicit, and on the verso of the last folio, is an inscription in a somewhat similar, but later, hand to the rest of the book. This inscription we reproduce in facsimile and transcribe as follows:



SUBSCRIPTION TO MS. BRITISH MUSEUM, SLOANE 2426, WRITTEN IN AN EARLY FIFTEENTH CENTURY HAND.

he was especially useful on account of his knowledge of Oriental languages.

The legend which we give below of the coming of Constantine to Salerno is no less improbable than that of Peter. It is perhaps a variant from the same original. The MS. from which it is taken was probably written about two hundred years after the death of Peter, in the days when the school of Salerno had declined and its place had been taken by Montpellier. We give the story as a legend and for what it is worth; it at least has a humorous aspect and yields us a glimpse of the way Constantine was regarded even by an unusually rational and scientific mediæval writer.

II. THE MANUSCRIPT.

The MS. containing our legend is in the British Museum and is numbered Sloane 2426. It is of octavo size and consists of 122 folios written closely and all in the same regular but very contracted hand. The volume bears the title "Copho Theoria Medicinæ. Anatom. Methodus Medendi." The work is, however, clearly not from the hand of Copho, who was a physician at Salerno in the eleventh century, but is of later date, though it relies largely on Salernitan sources. An in-

Barnarde de meerloe nativitas tua
fuit i(n) yselstein. anno d(omi)ni. M^oCCCC^oI^o i(n)t(er)
p(ost) festu(m) s(an)c(t)i remigii
q(u)inta(m) & sexta(m) ferias ^ di(mi)dia hora an(te) me-
dia(m) noctem. sol. (e)n(im). fuit planeta tuus. &
luna fuit in. XX^o. g(radu) lib(ræ). pat(ro)ni tui fuer(un)t
d(omi)n(u)s de egmonda. florentius de alkmae et
angela uxor gerardi de ema apoteharii.

Bernard de Meerloe, thy birth was in Ysselstein in the year of Our Lord 1401 between the Friday and the Saturday after the feast of Saint Remigius, half an hour before midnight. The sun was thy planet, and the moon was in the twentieth grade of [the zodiacal sign] Libra. Thy godparents were Master de Egmond, the notable of Alkmaar and Angela, wife of Gerard the Apothecary of Emmer.

The entry is a nativity and is of the sort made for the subsequent casting of a horoscope. It is not unusual to encounter entries of this kind in mediæval medical manuscripts. This nativity gives us at once the year 1401 as the terminus *ad quem* of the MS.

But the MS. was written at a considerably earlier date. At the beginning of the fifteenth century anatomy was deeply under the influence of the northern Italian schools, and

qua repare. tñsistit pñcept salerni qñ morbo afflictus
qñ infinita i medicos expendisset qñ tñsistit rñtate cari-
ores pñcept habebant. a nullo curat fñat. quē intuent
stamin' ait. Si me ab h' conoy pñcepto libatñs. ego a lan-
gore te libabo. Qui subridens credñs ipm deliquisse qñ
captiuū & ulli uestro inditū uidebat. nesciēs qñ i uñi ua-
le mirabile uñiū gñeat odore & cui omñs facient. i uñi
coipe magna scia latere possit. mñq. Tu imminenti pñcepto
qñ corñs pñcepto iā factus medic' libari uelles. n' credens
medicū ēē ipm. Tñ si ita ē ut testatñs pñcepta in aliq' eis
infirmitate decñto curatione. scō in me tñsistat. Et
factū ē sic. Cum pñcept. curat qñ di qñ hñc artē pñceptan-
tñm ad nos uolebat tñsistat. pñcept. Deñ uñq. tñm fa-
mos' cñ i multo honore a xpianñs habet' fact' ē & xpianñs
& pñcepta monach' cassinens' monach'. In salerni pñceptu sibi
i pñceptu medicū ē sacta. n' usq; in hodiernū diē ei gesta
referunt'. S; iā senio dissoluta a modernñs tñsistat sub ūbra
scientie possidñt'. S; in h' scie pñceptu extñs palmitib;
usq; ad mōtē pessulāū celeberñme ibid' renascit'. Iā tñp'
amonet pñcepta solue. pñcepto de ligamñtis qñ pñcepta mñcu-
loz iā pñcepta tñuoz disputatione.

De ligamñtis

Ligamñtū ē sūba int' ūuol atq; ossa media. sñā & sñā
ossib; mollior. tñm si durior. Incipit ab extñmitatē ossū
& nullū hñt sensū. qñ omñs qñ sensū hñt a cēbro pñceptunt
& rō fuerit necēria. tñt ligent ossa in gñatñatōē suā. t
ut lacert' cñ ossib; pñcepta ligñt. Coz forma ē diūsa. a' enī ē
rotunda sic ūuoz forma. qñ i locis ūuol carentib; sñ pñcepta
sñ in gñatñatōē armñ & cubita. a' sñ lata ut ligñda
sñ culec' & sñmñt ligent ligñda. a' sñ lata & subñlia sic
pñcepta atq; pñcepta uene artē. atq; ūuol defendunt'. Cubitales
enī corde & lacti tñuoz sñ hñt pñcepta sñ defensozib; co-
opta. & sñmñt alij loci hñt sñles.

De cordis

Corde sñ int' ligamñta & ūuol medie. qñ aligamñtis ossū
& ūuol lactos pñceptatib; sñt. Cñ enī ūuol ad lactos pñceptat
gñdiant in qñs diuidñt'. Cōmñtiones hoz lacti uocñt'

the work of Mondino (died 1327) or that of his pupil's pupil, Guy de Chauliac (died 1368), were the usual text-books. The author of our MS., however, though he devotes a large amount of attention to anatomy, not only refers to neither of these authors but shows no trace of their influence. This is the more noteworthy as Guy de Chauliac was early translated into Flemish. Our author, on the other hand, is familiar with the schools of Salerno and of Montpellier where Guy was professor, and he tells us that the former is in decay and has been replaced by the French University. After Hippocrates and Galen he refers most frequently to Theophilus. He is under definite Arabian influence, though he mentions only Avenzoar and Ali. He is familiar with, but very opposed to, certain Jewish physicians whom he does not name. These considerations, as well as palæographical appearances, prompt us to place the manuscript as dating from about the first third of the fourteenth century. The extreme limits are probably fairly represented by the dates 1310 and 1340. Palæographical grounds render it unlikely that it was written much before the former date and the contents of the MS. deter us from extending the latter date.

As regards the provenance. The places mentioned in the subscription are all of them within a small area in or near the province of North Brabant. Meerloe is in Brabant on the Maas, some thirty miles from Crefeld. The Yssel or Ijssel is a river which anastomoses with the northern mouth of the Rhine, and Ijsselstein is a very small town on the Ijssel near Utrecht. Ijsselstein is still a well-known surname in Holland. Alkmaar is a more important town in North Holland, about twenty miles north of Haarlem. Emmen or Emmer is a name given to several towns, small villages and hamlets in the province of North Brabant and in the neighboring provinces of Gelderland and Overijssel. It thus seems probable that our MS. was written, somewhere in the region of North Brabant, in the first third of the fourteenth century, while the subscription shows that it was certainly in use there in 1401.

III. THE TEXT.

SLOANE 2426.

[folio 7 verso line 31] de partibus musculos seu lacertos componentibus disputabimus. qui sunt ligamenta. caro. nerui. atque panniculi. quibus muscoli uestiuntur. etiam de aliis partibus corpus componentibus. ut sunt uene. & arterie. ossa. & de quibusdam superfluitatibus corpus honestantibus & iuantibus. ut sunt ungues & pili. ut ratio anatomie tocus [folio 8 recto] corporis sit euidetior. tractare non pretermitemus secundum auctoritatem Galeni & albansoardi cordubensis qui pantegni composuit. quamvis constantinus ipsum composuisse initiatur. tamen ipsum constantinus. & stephanus nepos patriarche antiochensis transtulerunt. Unde constat ipsos non fuisse auctores. & [5] inventores. sed tamen interpretes & expositores. ut theophilus fuit expositor libri urinarum quod ipse indicat tituli impositione. Uerumtamen cum ipse albansoardus inter omnes medicos cordubenses summus. qui erant numero mille. CCCC^{ta}. haberetur. plures discipulos habuisset. inter quos

sapientiores erant constantinus. & ali. filius tabernarii. qui iussu & [10] auxilio sui magistri. uiaticum. dietas utrasque. librum stomachi. chirurgie. librum graduum. & quamplures alios composuerunt. accidit. ut rex cordubensis qui lingua illa almansor dicitur. longe a ciuitate infirmaretur. qui cum adalbasoardum legatos ut cito ueniret misisset. tanquam dedignans uenire quia sapientia & nobilitate polle[15]bat. finxit se infirmari. & misit constantinum & ali. qui cum circa regem euigilantur & multo studio plura ex ratione fecissent. purgato corpore ut quartana omnino expellerent. ipsi in balneo posito opium in nimia quantitate constantinus obtulit. & benefecit. quia opium dedit sed male. quia quantitatem facila [? for facile] uirium conparationem non considerauit. tandem [20] cum ad ipsum venisset. prorsus humore congelato ne deinceps ad locum putrefactionis flueret. & spiritu frigidity opii extincto. omnino curatum inuenit. nil mali sentiens. que uidens timens usque in ultimum diem sibi sociari & in sepulcro poni. iniunxit circumstantibus ne streperent. & quiete essent. quia [25] rex dormiebat. & liberaretur in breue. Quod minime suo indicans socio qui circa spatiandi uillam exierat. amotis sarcinis & omnibus libris nemine sibi socio iuncto portum uenit. ubi casu nauem remis & uelo paratam prospero succedente uento littora relinquire inuenit. & cum itinere unius diei naute maria sulcassent. [30] ut credo nutu domini & eius prouidentia qui hanc artem in xpistianos transferre uolebat ad medelam ipsorum a salernitanis nautis causa prede maria solito transfretantibus sunt captiuati. & salerni deducti. & ut mos est captivorum uenales per uillam ducti. de quorum numero constantinus existens. a quodam coriario emptus est. qui constantinum suo negotio destinauit. quem cum contigisset iuxta littus maris [folio 8 verso] coria reparare. transiuit. princeps salerni graui morbo afflictus qui cum infinita in medicos expendisset qui tunc temporis raritate cariores prophetis habebantur. a nullo curatus fuerat. quem intuens constantinus ait. Si me ab hoc coriorum periculo liberaueris. & ego a lan[5]guore te liberabo. Qui subridens credens ipsum desipientem quia captiuum & uili ueste indutum uidebat. nesciens quod in uili uase mirabile uinum contineatur odore etiam cuius omnes sacientur. & in uili corpore magna scientia latere possit. inquit. Cum iminenti periculo quo torqueris periculo iam factus medicus liberari uelles. non credens [10] medicum esse ipsum. Cum si ita est ut testaris prius facta in aliquo eadem infirmitate detento curatione. secundo in me transferas. Et factum est sic. Curatur prior. curator gratia domini qui hanc artem per constantinum ad nos uolebat transfundere. & princeps. Deinde ubique cernitur famosus cum in multo honore a xpistianis haberetur factus est & xpistianus. [15] & pos[t]ea montis cassinensis monachus. Inde salernus primatum sibi in primum medicum est sortita. ubi usque in hodiernum diem eius gesta referuntur. Sed iam senio dissoluta a modernis ibi sub umbra scientie possiduntur. Sed inde huius scientie propaginum extensis palmitibus usque ad montem pessulanum celeberrime ibidem renascitur. Iam tempus [20] amonet promissa soluere. & primo de ligamentis qui sunt partes musculorum iam permissa neruorum disputatione.

IV. TRANSLATION.

We will now discuss the parts that enter into the composition of the muscles or brawns, namely, the ligaments, the flesh, the nerves, the fasciæ which cover the muscles, and also other component parts of the body, such as the veins, the arteries and the bones, and certain accessory adornments and accessories of the body, such as the nails and hairs.

In order that our general anatomical account may be the clearer, we will treat of it according to Galen and Avenzoar the Cordovan who composed the *Pantegni*. The beginning of this book was the work of Constantine and he, together with Stephanus, the nephew of the patriarch of Antioch, translated it. On which account it is well known that they were not authors or discoverers, but mere interpreters and expositors, like Theophilus, who was but an expositor of the *Liber Urinarum*, as he himself indicates by the borrowed title.

However that may be, this Avenzoar was regarded as the greatest of all the physicians of Cordova who were no less than fourteen hundred in number, and he had many disciples. Among these the wisest were Constantine and Ali, son of the tavern-keeper, who, with the help of their master, composed the *Viaticum*, the two works on Diet, the *Book of the Stomach*, the *Surgery* and the *Book of Steps* and a number of other works.

Now it happened that the king of Cordova, who in their tongue was called Almansor, was taken ill when far from home, and he sent messengers to Avenzoar that he should come quickly [to his aid]. He, however, being a powerful man by reason of his wisdom and his noble birth, scorned to go but pretended to be sick and sent Constantine and Ali instead.

And they watched by the king's bedside and wrought mightily according to their art and his body was purged so that the quartan fever was wholly expelled therefrom. Then when he was in his bath Constantine exhibited a large quantity of opium. Now he did well in that he gave opium, but he did ill in that he did not estimate exactly its amount and strength. At last, however, [the king] came to himself [again]—the humor being completely solidified and its essence destroyed by the frigidity of the opium—and he felt no ill effects.

Seeing this and fearing that he would be tethered to him for his whole lifetime and until his death, [Constantine] conjured the attendants to make no noise but be still, for the king slept and would shortly awake healed. And without notifying his companion [Ali] who had gone for a walk round the town, and with neither baggage nor books nor friend, he made his way to the harbor, where, by great good luck, he found a land breeze blowing and a ship with oars in readiness and sails set.

Now, when they had cleft the waves for the distance of a day's journey, they were held prisoners by the Salernitan sailors, for the sake of gain, as is the custom with these cross channel seamen. And this was done, as I believe, by the will of God and through the providence of Him who wished to bring this art to the Christians to heal them. And when they had reached Salerno, they were led for sale through the town

after the manner of captives. And Constantine, who was of their number, was purchased by a dresser of hides who wanted him for his trade.

It happened that one day he was dressing skins by the seashore when the prince of Salerno passed by. Now the prince was stricken with a grievous sickness and had spent vast sums on physicians, who in that age by reason of their rareness were cherished above prophets, but by none of them had he been healed. And Constantine, when he saw him, spake thus: "If thou wilt free me from the misery of this skin-dressing trade, I will free thee from thy sickness." But the prince smiled, thinking him a madman, for he saw that he was a captive and poorly clad and he knew not that wine of the most satisfying quality and delicious bouquet may be contained in the poorest of flasks and that vast wisdom may rest in a mean frame. Not believing him to be a physician [the prince] therefore said: "Thou that claimest to be a physician and wishest to be delivered from this squalor in which thou liest, if it is as thou sayest, first thy cure shall be wrought on some sick prisoner and afterwards on me."

And it was so; first [the prisoner] and then the prince was cured, and cured, mind you, by God's own grace, who willed to bring us this art through the agency of Constantine. Wherefore is he [Constantine] everywhere well regarded and held in great honor by the Christians. And afterwards he himself became a Christian and a monk at Monte Cassino. Wherefore at Salerno he is regarded as the very first of physicians and there, unto this day, they speak of his works, though now, decayed with age, they are considered by the moderns as in the twilight of science. But that science has been reborn, and a young shoot has gone out from the old vine in the famous city of Montpellier.

But time warns me to redeem my promise and now I must speak of the ligaments which are part of the muscles.

V. COMMENTARY.

The story as here detailed contains so many improbabilities and anachronisms that it would be hopeless to attempt to find any new fact therein. We treat it as a legend, appending certain notes on the events and persons mentioned.

Avenzoar. The family of Avenzoar, Ibn Zohr or Ben Sohr, produced a large number of distinguished members and included several physicians whose lives and works are confused by mediæval writers. One of the Avenzoars, 'Abd Al Malik ibn Zohr ibn 'Abd Al Malik (Abú Merwan), was born near Seville about the beginning of the twelfth century. He passed into the service of the mulatto Abd al Munim and as the latter rose to sovereign power Avenzoar also became very wealthy and distinguished. This Avenzoar died at Seville in 1162. His work "*alteisir*—[*facilitatio seu adjumentum scilicet regiminis et medilae*]" was eight times printed in Latin between 1490 and 1574, always with the *Colliget* of Averroes. The Latin version is itself from a Hebrew translation, which has perhaps given rise to the widespread, but erroneous, impression that Avenzoar was himself a Jew. Another work of

Avenzoar on "The cure of stone" was printed in Venice in 1497.

The Pantegni (παντέχνη) was the work not of Avenzoar but of Galen. A rendering of it is attributed to Constantine.

Stephanus, the nephew of the Patriarch of Antioch. Under this name our author is confusing two writers. *Stephanus of Athens* (seventh century) who was a pupil of Theophilus (Philaret) lived in Byzantium, and afterwards in Alexandria. He produced a work on fevers, and the work on urine attributed to Theophilus was probably his. On the other hand, *Stephanus of Antioch* translated, in 1127, the works of Haly Abbas. The folio edition of Haly Abbas, printed at Venice in 1492, opens thus (folio 6 recto) "Incipit prologus Stephani philosophi discipuli in libro medicinae qui dicitur regalis dispositio quem ex arabico in latinam transtulit facultatem."

Ali, son of the tavern-keeper, is also clearly the result of the confusion of two Arabian writers of that name, Ali ben Redhvan and Ali ben Abbas. Ali ben Redhvan, the Haly Rodoam of mediæval writers, was the son of a water-carrier. He was born at Kahira, became physician to the Khalif El

Halim, and he died probably in A. D. 1061. A Latin translation of a work of his was published at Venice in 1496, as "Commentarius in artem parvam Galeni" (ars parva = microtegni = ars medica of Galen). Ali ben Abbas, on the other hand, the Haly Abbas of mediæval writers, was a Persian physician who died A. D. 994. He wrote a work entitled *Almaleki* (= Liber regius) which had great influence on mediæval writers. This was probably epitomized by Isaac Judaeus and from his compilation translated by Constantine. It is included in the Basel edition of Constantine's works (Henricus Petrus, Basel, 1536 and 1539).

Almansor is a further confusion. The liber medicinalis *Almansoris* (ketaab altebb *Almansura*) was the work of the Persian Rhazes (died A. D. 923-4). It had its name from the dedication to the ruler of Chorasán. The ninth book of the *Almansur* (nonum *Almansoris*) was especially popular in the middle ages. It was widely used as a text-book of pathology and therapeutics, was very frequently translated and commented upon, and a large number of early printed versions are known.

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REGENERATION IN PERIPHERAL NERVES.* AN EXPERIMENTAL STUDY.

By EDWIN G. KIRK, M.D., and DEAN D. LEWIS, M.D., Chicago.
(From the Morris Institute of Medical Research of Michael Reese Hospital.)

In a previous communication¹ it was shown that nerve defects may be bridged successfully by tubulizing with an autotransplant of fascia. Although devised primarily with reference to practical surgical use, it soon became apparent that the method afforded unusual opportunities for a study of the histology of nerve regeneration following mechanical trauma. Fig. 1 (A and B) illustrates the technique employed, which is described in detail in the article referred to. The defect is produced by excising a segment, varying in length from 1 to 3 cm., the nerve being cut squarely across with a sharp knife. Fascia lata from the same animal is used to construct the tube, since by using an autotransplant fibroblastic reaction and subsequent cicatrization are avoided. Thus regeneration following trauma may be studied without interference from various external factors and in particular the ingrowth of cicatricial tissue between the ends. Most important of all, the comparative behavior of proximal and distal stumps is more easily determined than when the ends are approximated.

MATERIAL AND TECHNIQUE.

The material used in the present report includes 41 sciatic nerves of adult dogs, 21 of which are in complete serial section. The animals were killed at periods varying from one day to 36 weeks after operation. In general, four methods of histological preparation have been employed: (a) Fixation in Bensley's fluid (Müller's fluid saturated with mercuric bichloride and with 10 per cent of formalin added just before use) and staining in Mallory's phosphotungstic acid hematoxylin. Myelin sheaths are stained an intense blue; the axis-cylinders are unstained or are light blue; the chromatic elements of neurilemmal and other nuclei blue; and connective tissue red. (b) Cajal-Ranson silver impregnation—following Held's pyridin technique. The non-medullated fibers are an intense black, the axis-cylinders of medullated fibers a yellow brown, and the general background of tissues a light yellow. (c) Hematoxylin and eosin—especially in the study of protoplasmic bands. (d) Often the silver preparations were counterstained with safranin.

THE EARLY STAGES.

An exudate of serum into the empty fascial tube begins on the first day. At the end of 72 hours the tube is partially filled with serum containing a few mononuclear migratory cells. If hemostasis has been adequate, there will be prac-

* Read before The Johns Hopkins Hospital Medical Society, April 3, 1916.
¹ Fascial Tubulization in Repair of Nerve Defects. Sect. Surgery, A. Med. Assoc., San Francisco, June, 1915; J. A. M. A. 1915, LXV, 486-491.

tically no erythrocytes. By the fifth day the portions of the tube nearest the two nerve stumps are filled with a soft grayish-white pulpy material, resembling in appearance soft brain matter. The exudate comes from the nerve ends, the fascia showing no reaction. Microscopically this pulpy material is finely granular and homogeneous—evidently coagulated lymph. Sometimes the middle portion of the tube, the part most remote from the divided nerve ends, is still empty on the fourth or fifth day.

EARLY CHANGES IN AXIS-CYLINDERS AND MYELIN SHEATHS.

On the basis of his own observations and those of others, Ranson (1912) comes to certain conclusions which we have been able to confirm. We shall, therefore, give them only a brief consideration, referring the reader to his work for details. In both stumps there occur during the first two to three days abortive regenerative changes, manifested in the outgrowth of fine terminal and lateral neurofibrillar rami from non-medullated as well as from medullated axis-cylinders, in the dissociation of the axis-cylinders into bundles of fine neurofibrillæ, and in the development of delicate plexuses of such fibrillæ beneath the neurilemmal sheaths. These abortive fibers appear in the proximal and also in the distal stumps, but only in the immediate vicinity of the section (a few tenths of a millimeter). They degenerate completely in from three to eight days. Ranson has demonstrated the temporary nature of these phenomena in the distal stump, where they have often been mistaken for definitive regeneration. Certain degenerative phenomena also develop early. In both stumps the axis-cylinders and myelin sheaths of medullated axones degenerate for a distance of about 0.3 mm. (second to third day). The non-medullated fibers of the central stump also exhibit a slower, ascending degeneration (third to eighth day), which extends upward for about 1 cm. The Wallerian degeneration, occurring later, is somewhat slower, and is observed in the whole distal segment—the axis-cylinders becoming swollen and fragmented (second to fourth day), and the degeneration of the myelin sheaths quickly following (fourth day). Definite regenerative changes occur in the central stump only. By the eighth day the medullated fibers have given off numerous lateral rami higher up (5 mm. and less from section), these growing down as subneurilemmal fibers within the old sheaths. The non-medullated fibers also dissociate into bundles of neurofibrillæ, which grown down in the sheath (by the fourteenth day). At the end of one month all the medullated and non-medullated fibers in the last 5 mm. of the proximal stump have been converted into bundles of non-medullated fibers, each bundle containing from 20 to 60 fibrillæ or more. These are much more numerous than in the normal nerve. Ranson suggests a teleological explanation of this hyperregeneration—with special reference to the number of fibers which must later go astray in the scar.

CHANGES IN NEURILEMMAL SHEATHS.

As is well known, the adult neurilemmal sheath (Schwann) of peripheral nerves is a fine, thin, structureless membrane

almost invisible and provided with a very few, fusiform nuclei—one to each node of Ranvier, the length of the latter varying from 80 to 900 μ . The nuclei are surrounded by a very small quantity of cytoplasm. Mitoses are not present in the resting stage. Fig. 2 illustrates the maximal number and the appearance of neurilemmal nuclei in an adult peripheral nerve. It is rarely possible to find so many in one field. Note that the cytoplasm is practically invisible.

We believe that the phenomenon now to be described is of the greatest importance in the regeneration, or attempted regeneration, of nerves. We refer to the very early reaction of the neurilemmal sheaths adjacent to the point of section of both proximal and distal stumps. This is a hyperplastic reaction, the adult (resting) neurilemmal sheath, with its nuclei, reverting to the active or embryonic type. The first indications of this activity are seen in a slight increase in the amount of granular cytoplasm surrounding the nuclei, or rather a becoming visible of the previously invisible cytoplasm. We have seen this first between the twenty-fourth and thirty-sixth hours in the portions of the neurilemmal sheaths closest to the level of section. This earliest change is demonstrable only with difficulty. The cytoplasm surrounding these nuclei increases rapidly in amount the next two days, and the nuclei increase rapidly in number by mitosis, so that between the fourth and sixth days the protoplasmic bands (the primitive *Bandfasern* of earlier authors) become well developed (Fig. 3). These are narrow strands or bands of cytoplasm containing the now hyperchromatic and active neurilemmal nuclei. By the fifth or sixth day numerous protoplasmic bands have already invaded the serum of the fascial tube, and from that time on they proliferate continuously down the tube. Fig. 4 shows the bands running down into the serum from the proximal stump. At their point of origin—namely, in the last .2 or .3 mm. of the proximal stump, they constitute thickened bands of cytoplasm within the neurilemmal sheaths. Their relation to the resting neurilemmal sheath is shown diagrammatically in Fig. 1, *c*, in which (*a*) represents the neurilemmal nucleus, (*b*) the thickened cytoplasm, constituting, as seen in longitudinal preparation, the *Bandfaser* or protoplasmic band, and (*c*) the non-hypertrophied parts of the sheath, the whole presenting the appearance of a seal-ring.

Thus the position of the nucleus determines the point of development of the band within the sheath. As soon as the band leaves the nerve stump and goes down into the serum, it appears as a solid, somewhat flattened, strand of cytoplasm, not as a tube; for the thin portion (*c*) either atrophies, or more probably collapses, and fuses with the protoplasmic strand, obliterating the lumen of the sheath.

In preparations such as are represented in Microphotograph 4, it is important to observe that these protoplasmic bands are traceable in absolute continuity from the terminal portion of the stump down into the serum of the tube. The transplanted fascial tube at this, as at all levels, displays no fibroblastic reaction.

Fig. 3 shows an area ($\times 1000$) from the proximal stump 2 mm. above the plane of section on the sixth day. Note be-

tween the large medullated fibers, the slender protoplasmic bands with numerous neurilemmal nuclei, some having just divided—all rich in chromatic material.

Fig. 5 shows in detail an area from the same nerve at the very tip of the proximal stump. Note the swollen degenerated medullated fibers and sheaths, and between them the protoplasmic bands with their neurilemmal nuclei.

Precisely the same phenomenon occurs in the distal stump. Fig. 6 is a low-power picture ($\times 335$) of the proximal end of the distal stump of the nerve represented in Figs. 3 and 5. Note the swollen degenerated medullated fibers and sheaths (*a*) and between them the hyperplastic neurilemmal bands (*b*), the latter also growing up into the serum of the tube at *c*.

Fig. 8 shows an area of the same distal stump just below the plane of section. Note here again the large swollen fragments of medullated axis-cylinders and their myelin sheaths, the material of the latter clumped as "ovoids," in the midst of which are the semi-digested remnants of the axis-cylinders. Between them are the hyperplastic neurilemmal nuclei and their bands of protoplasm (*a*). The latter are not quite as numerous or as well developed as in the proximal stump. Fig. 7 shows the very tip of this same (distal) stump, illustrating the additional feature of the growth of bands into the serum at *a*. Here also may be seen fragments of degenerated axis-cylinders surrounded by the "ovoids" of myelin (*b*). Although this outgrowth of neurilemmal protoplasmic bands occurs at both the proximal and distal stumps and is of a similar nature in each, it is much more active at the proximal end. Thus the bands rapidly progress into the serum from the proximal end, and much less rapidly from the distal, so that they meet at a point much nearer the distal than the proximal stump. The approximate rapidity of growth is indicated by the fact that, after removal of a segment 12 mm. long (Nerve 79), the protoplasmic bands have completely bridged the tube of serum by the sixth day, being very numerous near the proximal stump (Figs. 3 and 5), much less numerous near the distal stump (Figs. 6, 7 and 8) and least numerous at a point about 10 mm. from the end of the proximal and 2 mm. from the end of the distal stump (Fig. 9). This last level represents the meeting point of the two sets of protoplasmic bands. All these phenomena occur earliest in the last millimeter of the proximal and the first millimeter of the distal stump. On the sixth day the process is most marked, that is, the protoplasmic bands are largest and most numerous, and their nuclei most hyperplastic, at their very tips. At a distance of 1 mm. from the tips the process is decidedly less active, that is, the nuclei, although many times more numerous than in the normal nerve, are yet strikingly less so than at the very tip, and the protoplasmic bands are not so long or numerous. At a distance of 2 mm. there is still a decided increase in the number of nuclei and a considerable increase in the cytoplasm surrounding them as compared with the normal resting nerve, but no distinct band-formation. This applies to both stumps. In the lower stretches of the distal stump, more than 2 mm. from the plane of section, the hyperplasia of nuclei is not very evident until the fourth day, and the protoplasmic

bands are not well formed until the ninth day and later. It will be noted below, in the review of the literature on neurilemmal hyperplasia, that we describe this phenomenon as developing at a time considerably earlier than that noted by various other investigators. Thus we find that well-formed protoplasmic bands have invaded the exudate in the tube as early as the fourth or sixth day, whereas others describe them as appearing first about the eighteenth or twenty-first day. The explanation of this apparent discrepancy has already been hinted at. The process of hyperplasia is essentially of the nature described throughout the whole of the distal and the lower end of the proximal segments, but certain factors, doubtless largely the mechanical trauma, greatly accelerate the process in the last millimeter of the proximal and in the first millimeter of the distal stump. In the immediate vicinity of the severe nerve injury, associated with a break of continuity, there occurs a special acceleration of the process of protoplasmic band-formation. It is obvious, from the facts recorded above, that this may be regarded as nature's effort for insuring a pathway for the regenerating axis-cylinders. In ordinary nerve repair this regenerative process is often interfered with by the ingrowth of extraneous cicatricial tissue. All former descriptions of the neurilemmal hyperplasia and formation of protoplasmic bands are based on the process as it occurs at a distance of a millimeter or more from the level of section. Doubtless, this is due to the fact that this outgrowth of neurilemmal bands was considered to be atypical, or that with the ordinary methods of approximation the cicatricial reaction obscured this feature of the process. No one to our knowledge has observed this accelerated neurilemmal hyperplasia occurring at the end of the segments. Ingebrigtsen's speculation as to the difficulty of finding such bands in the scar is suggestive in this connection. Of course the accelerated *degenerative* phenomena at this location have often been noted. Howell and Huber (1892) observed that, in the immediate neighborhood of the wound, degenerative changes of traumatic origin undoubtedly occur before they appear in the rest of the nerve. Ranson also mentions the rapid traumatic degeneration in the immediate vicinity of the plane of section.

MORPHOLOGY OF THE BANDS.

The protoplasmic bands, as they grow down into the serum, anastomose frequently. This is best demonstrated by a serial study of cross-sections (of which Fig. 13 shows one); but it is also seen in the longitudinal preparations (Figs. 9, 10, 11). The anastomoses are much better demonstrated on the corresponding specimens by focussing in various planes. In Fig. 9 the most conspicuous elongated band (*b*) is seen branching just as it leaves the plane of the section. Sometimes, however, the bands run for about 100-200 μ without anastomosing (Fig. 12). These bands are often very difficult of demonstration, as their cytoplasm does not stain well. Sometimes they are rendered visible by the silver technique, taking a faint yellow color. In general, the best preparations were obtained with hematoxylin and eosin, or with safranin.

The recent observations of Ingebrigtsen (February, 1916) are of interest in this connection. On incubation of peripheral nerves in plasma, a growth of the sheath of Schwann occurs, provided the axis-cylinders and myelin have undergone Wallerian degeneration previous to the implantation. There is a striking resemblance between the neurilemmal bands as we find them in the serum of the fascial tube, and the ones pictured by Ingebrigtsen.² After three to four days' incubation in plasma, there grow out from the cut ends of the nerve fibers numerous thin filaments of protoplasm, highly refractile and slightly granular. At first they are tapering, and end in a point which shows amœboid movements, by means of which they emerge into the plasma. They soon become more or less cylindrical, and branch and anastomose. The average width is 6 to 8 μ . The bands contain nuclei of an elongated ovoid or fusiform shape. Inasmuch as the nuclei are slightly greater in diameter than the protoplasmic band, the latter shows a slight expansion at the site of each nucleus. After six days' incubation the bands anastomose very freely. As in our preparations, there are often stretches of such bands measuring 200 μ or more in length, devoid of nuclei (Ingebrigtsen's Fig. 4). In the summary Ingebrigtsen speculates as follows: "Is this an indication that such an outgrowth occurs from the cut end of a degenerating nerve in the organism, and plays some part in the processes of union and regeneration? I have never seen it, and I am not aware that it has been noticed by other observers. But it is probable that such a growth from the cells of Schwann of the peripheral part of a divided nerve extends into the scar tissue forming part of it. That structures of this kind have not yet been detected in the organism does not prove their non-existence. They stain faintly, and curving and bending through the scar tissue it may be difficult to bring out their true form." In a critique of neurotropism he says: "An anatomical conception of the centrifugal orientation, based upon my experiments, seems more satisfactory, assuming that the protoplasmic syncytium of Schwann growing out from the peripheral part of a divided nerve, branching into the scar, may receive the axis-cylinders coming from the central part, and serve as a guidance for them into the peripheral segment."

We had already (Kirk and Lewis, December, 1915, and January, 1916) answered these questions affirmatively.

Stellate and branching connective-tissue cells are also found in the serum of the tube near the nerve stumps. They are derivatives of the endoneural connective tissue. Ingebrigtsen observed these along with the neurilemmal bands in plasma cultures. Lymphocytic migratory cells also find their way into the serum of the tube (see Fig. 9).

Nageotte (1911) has shown the adult (resting) neurilemmal sheath to be a syncytium. Ingebrigtsen's observation (1916) that the test-tube growths of neurilemmal bands show frequent anastomoses after a few days' incubation, while the axis-cylinders never do, is of significance in this connection. This feature of the structure is brought out in relief in the

hyperplasia, even in those parts removed from the sectioned ends, the protoplasm of adjacent sheaths being continuous. We have already referred to the frequent anastomoses in the bands as they grow into the serum. Thus it seems to us a misconception to speak of the protoplasmic bands as appearing on the fourteenth day or on the eighteenth day by fusion of the previously isolated masses of cytoplasm. From their inception they form a continuous plexus that simply becomes more protoplasmic as hyperplasia advances. This is the first time, so far as we are aware, that the tubulization technique with separation of the two nerve ends has been applied to the study of the behavior of the protoplasmic bands. It has, of course, long been recognized that at some time (two to three weeks) after the initial trauma, the hyperplasia of neurilemmal nuclei and associated cytoplasm gives rise to the formation of the so-called "primitive Bandfasern," both in proximal and distal segments.

Büngner's observations (1891) are of unusual interest. Unfortunately, owing to the use of the inferior technique of that day, he erroneously interpreted certain longitudinal striations appearing in these bands in the distal segment as representing new axis-cylinders developing by peripheral regeneration, an error hardly possible with the use of the silver technique (see Ranson for a critique of Büngner's work). Büngner's descriptions and figures of the protoplasmic bands are very accurate. On the third day after crushing or cutting of the nerve the nuclei of Schwann in both proximal and distal stumps become hyperplastic and divide by karyokinesis. Cytoplasm accumulates about them on the inner surface of the thin sheath, and that surrounding the individual nuclei rapidly forms bands by fusion. Nuclear activity is at its height between the fifth and eighth days. Cross-sections of these bands often show (*e. g.*, his Fig. 10) the typical seal-ring appearance mentioned above. Myelin fragments are, as usual, often present in the protoplasm of the bands.

Howell and Huber (1892) describe hyperplasia and proliferation of the neurilemmal nuclei and associated cytoplasm on the seventh day, at points some distance distal to the level of the section. On the twenty-first day they find well-developed "embryonic nerve fibers" (protoplasmic bands). These develop in the central and peripheral segments and arise from the neurilemmal cytoplasm. They make the important observation that the regenerating axis-cylinder is found in the embryonic nerve fibers of the proximal stump. They also find them within the same bands of the distal stump. They speculate as follows: "How is the connection between the two made? It is practically an impossible thing to witness the making of this connection, but we are strongly convinced that it takes place in the cicatricial tissue, and chiefly from the downgrowth of embryonic fibers from the central end." Speaking of the intervening scar they say: "It forms a tissue into which the actively growing embryonic fibers from central and peripheral ends penetrate, and finally meet and unite" (p. 384). They made the observation (confirmed by Ranson in 1912, and by us) that, if the cicatrix prevents union of the two ends, the protoplasmic bands still form in the distal

² Compare, for example, Ingebrigtsen's Fig. 3, plate 34, with our figures.

stump, this being then the sole manifestation of peripheral regeneration.

Our present work not only confirms Howell and Huber's as to the absolutely autochthonous formation of the bands in the proximal and distal stumps, but also shows that, before any axis-cylinders grow from proximal into distal segment, the bands must grow across the gap (or cicatrix), and prepare the way. (See section below on "Neurilemmal bands as pathways.")

Huber (1892) studied the behavior of neurilemmal nuclei after section of nerves in rabbits. At two days the nuclei are enlarged, ovoid, hyperchromatic and surrounded by an increased amount of cytoplasm. Mitoses are present at the end of the third day. The distribution of the dividing nuclei throughout the Ranvier segment is believed to be due to an active motility of nucleus and adjacent cytoplasm.

Huber (1895) describes in implanted nerve segments a similar hyperplasia of neurilemmal nuclei, but not so marked as in the distal segments. After from six to nine days the neurilemmal sheaths are described as much collapsed, containing a little cytoplasm and a few nuclei.

Ballance and Stewart (1901) describe and figure a marked proliferation of neurilemmal cells beginning on the second day (their Figs. 1 and 2, Pl. 15). They lay no emphasis on any functional activity of these cells until later stages are reached. Ranson (1912) finds typical protoplasmic bands in the distal segment on the nineteenth day, developing from medullated and non-medullated fibers.

THE NEURILEMMAL BANDS AS PATHWAYS FOR AXIS-CYLINDERS.

Our observations prove conclusively that the protoplasmic bands constitute conduits, in the substance of which the non-medullated fibers of regeneration from the proximal stump rapidly grow down (Figs. 10, 11, 12 and 13).

On the sixth day such axis-cylinders are already found in many bands at a distance of 1 mm. from the extreme end of the proximal stump. Sometimes the fiber is well embedded in the cytoplasm, sometimes it lies very near the surface. We have best demonstrated these relations by impregnating with silver, and then rapidly counterstaining with safranin. The bands grow down first, and the nerve-fibers follow along them. This is determined in both longitudinal and cross-sections. In the former, many bands will be seen which contain no fibers. At the six-day stage the bands are found to contain fibers only in the first millimeter from the central end, although the bands have bridged a gap of 12 mm. The down-growing axis-cylinders will not completely bridge this same gap and reach the distal segment in less than three weeks. After four weeks numerous fibers have passed through a gap of about this extent and entered the distal stump (Fig. 20). In the serial transverse sections, except in stages so far advanced that neurotisation is complete across the gap, one can compare sections at the upper part of the tube, in which many or most of the bands contain axis-cylinders, with those from lower levels in which the bands are devoid of them. Photograph 13 was taken at such a level

that some of the bands show an invasion by axis-cylinders and some have none. The axis-cylinders are stained an intense black by the silver. Note the numerous neurilemmal nuclei as seen in cross-section. The bands first enter the serum as separate strands, but a little later anastomose to form a very complete rete. Thus it comes about that the bundles of regeneration from various axones often partially interlace (Fig. 19). Ranson (1912) also has described this condition (his Fig. 27).³

We do not wish to imply that the axis-cylinders always and necessarily track along the protoplasmic bands; for it is definitely known that, under special and unusual conditions, such is not the case. Ingebrigtsen (1913) cultivated cerebellar tissue *in vitro* (plasma media), and obtained growths of axis-cylinders. This result was confirmed later (Ingebrigtsen, 1913) by Cajal's silver method. They grow out into the plasma unaccompanied by structures of any kind, and do not anastomose. Here the advancing axis-cylinders were supported by a surface. The same experiments also showed outgrowth of neuroglia fibers as an anastomosing rete. Clark (1914) produced experimental polyneuritis (beri-beri) in fowls by feeding polished rice. Myelin sheaths and axis-cylinders of peripheral nerves were brought to any desired stage of degeneration. All traumatic and inflammatory effects, such as are produced by sectioning or otherwise interrupting the continuity of fibers, were thus avoided. Under proper diet, regeneration of axis-cylinders and myelin sheaths, the former always from the central end toward the periphery, could be induced. Only in the most advanced and prolonged degenerative changes of cylinders and myelin sheaths did he ever find multiplication of neurilemmal nuclei. Here again is an example of the down-growth of axis-cylinders without the aid of tracks in the shape of protoplasmic bands. In this case it is obvious that there is a tubule preformed for the conduction of each regenerating fiber. But while under such exceptional conditions nerve fibers may grow down independently of the bands, we are convinced from our observations that in regeneration following trauma—and such embraces practically all cases in which surgical intervention is indicated—a pathway across the cicatrix, or from proximal to distal stump in case of apposition of the ends, is prepared only by these bands. When they are deflected as by the cicatrix, the axis-cylinders following them are likewise deflected (Fig. 10).

We have already mentioned that Howell and Huber (1892) describe and figure the regenerating axis-cylinders as being situated within the embryonic nerve fibers of both proximal and distal stumps. Huber (1895) verifies the down-growth of axis-cylinders into the old sheath of Schwann, filled with cytoplasm, in the lower part of the central stump; also within and between the old sheaths in implanted segments; and in the same localities in the peripheral stump.

Harrison (1908) cut nerves in the tail of frog larvæ and found that the proximal and distal stumps of many fibers were united by strands of protoplasm on the second day. When this

³ Nageotte (1911) has shown the protoplasm of the neurilemmal sheath in the resting condition to constitute a syncytium.

occurred, degenerative changes in the peripheral segment were inhibited. These results are not surprising, in view of the great regulative power shown by tissues of lower vertebrates, and especially of larvæ. Ranson (1912) particularly emphasizes the use of protoplasmic bands of the distal segment as pathways for the invading axones. He finds the bands well developed on the nineteenth day, and new non-medullated fibers from the proximal stump already running in their proximal portion. *These axis-cylinders always run down in the bands, never between them.* Several axis-cylinders often lie within one band (his Fig. 29). Dustin (1913) believes that nerves heal by a special type of cicatrix formation. In the primary connective-tissue scar are organized paths of least resistance (Leitbahnen), through which the nerve fibers pass. This specific cicatricial tissue is found only between nerve fibers, and is derived from the connective-tissue cells of the nervous system. It rapidly forms a "porous callus," and unites the stumps provisionally but exactly. Nageotte (1915) discusses "the process of cicatrization in nerves" in a brief report, based on the study of two (2) nerves at the fourth week of regeneration. The nerves were sectioned; one was tubulized with a vein, the gap measuring 1.7 cm.; the other was bridged with silk, the defect measuring 1.4 cm. Each animal was killed after one month, and the nerve fixed in formalin and stained in iron hematoxylin and Van Gieson. He concludes that the young axis-cylinders grow down only in a syncytial network derived from the sheath of Schwann. He assumes the sheath to be of ectodermal origin, and maintains that the axis-cylinders never grow naked into the mesenchyme, but always surrounded by this ectodermal sheath, several axis-cylinders often within one sheath. The sheaths regenerate from both the proximal and from the distal stumps. He believes that the axis-cylinders cannot exist apart from the ectodermal sheath. It is difficult to conceive how Nageotte has been able to arrive at these elaborate deductions from two specimens each at the fourth week. We believe, however, that he has seen at a later stage the same phenomenon which we have seen in a series ranging from one day to 36 weeks. We cannot concede that the axis-cylinders and neurilemmal bands of the proximal stump grow down at the same time. The latter certainly precede the former.

Ranson (1912) and others have already abundantly demonstrated the origin of the new axis-cylinders from the stumps of non-medullated and medullated fibers. As they have shown, there is an immense over-production of fibers. This is illustrated repeatedly in our series. Fig. 14 represents a cross-section taken 2.5 cm. above the level of the proximal plane of section at six weeks. Note the enormous number of non-medullated fibers, interspersed among the medullated. Some are derivatives of non-medullated fibers, and some of medullated, as is illustrated in Fig. 15, in which (a) points to a subneurilemmal plexus derived from the medullated axone by lateral branching, and (b) to a bundle derived from a non-medullated one. All fibers of regeneration are at first non-medullated. Persistent nerve fibers grow down, as we have seen, into the protoplasmic bands of the tube as early as the fifth and sixth

days. Fig. 17 gives a detail from the intermediate (regenerated) segment at six weeks. Note the bundles of non-medullated fibers. Many of them as (a) illustrate the fact that the medullated fibers, in regenerating, not only give rise, higher up, to numerous lateral rami, that course down just beneath the neurilemma, or, better, within the protoplasmic band of the neurilemma, but also that the stump of the old central axone also grows down as one (or sometimes several) fibers. Fig. 16 shows the proximal stump just above the plane of section after 8½ weeks. Note the remnants of swollen degenerated medullated axones (a), and the large bundles of non-medullated fibers. Fig. 18 illustrates the fibers growing down through the intermediate segment. Note the arrangement in bundles. End-bulbs are seen on the growing tips of some of the fibers. Fig. 19 is from the intermediate segment and illustrates the arrangement in bundles, the fibers of which course along a single protoplasmic band. Note the deflection of some bundles corresponding with anastomoses of bands. The invasion of the distal segment by the regenerating fibers, as seen in silver preparations, is illustrated in Fig. 20 (four weeks), and in Fig. 21 (seven weeks).

Fig. 26 illustrates a phenomenon we have often observed in the distal stumps; namely, the persistence of certain elements of the old sheaths, as manifested in old resting nuclei (a) and fibrous connective-tissue strands, surrounding the sharply marked bundles of new fibers, mostly non-medullated (b) and hence appearing glistening white, and not sharply defined in the microphotograph; some, however, having acquired the new medullation (c). Interspersed among these fibers are the new (hyperplastic) neurilemmal nuclei (d). The resting nuclei (a) are either neurilemmal or connective-tissue nuclei—we are not yet certain which. If the former, then, it would appear that in the several weeks which elapse, in the case of a large defect, before axis-cylinders from the central stump reach the distal canals, the neurilemmal bands may go through their stage of hyperplasia and then revert to the resting stage, and that neurilemmal sheaths from higher up (as from the distal level of Section 1) may grow down with the axone. We suspect, however, that these resting nuclei (a) belong to the connective-tissue sheath of Henle.

The hyperplasia of neurilemmal nuclei persists a very long time. Langley and Anderson (1904) have already noticed this. Fig. 27 shows them in the distal segment after 30 weeks. The nuclei which are yet very large, hyperchromatic and numerous, are applied to the non-medullated and medullated fibers, of course in a subneurilemmal position. Fig. 26 also illustrates the persistence of embryonic neurilemmal nuclei (d) after 27 weeks.

BIOLOGIC INTERPRETATION OF NEURILEMMAL HYPERPLASIA.

The hyperplasia of neurilemmal cytoplasm and nuclei has been recently interpreted by certain authors as a degenerative phenomenon, occurring only in a nerve undergoing "progressive retrogression," this interpretation being based largely upon experimental work in which neurilemmal hyperplasia was

absent in moderate grades of axis-cylinder and myelin degeneration, and present in severe grades, as also in advanced generalized degenerative processes, for instance, in gangrene of an extremity. But, in observing the processes, both the rapid degeneration in the immediate proximity of the section, and the slower Wallerian degeneration, we cannot but be struck by the intimate association of retrogressive and progressive processes. As V. Büngner (1891) says: "The processes of degeneration and regeneration are so closely associated, both as to spatial and temporal relations, that they defy any separate consideration, occurring simultaneously and in the closest proximity."

Yet it is possible, just as in the case of the phenomena of inflammation, to be sure that certain phases of the complex process partake of the general nature of a degeneration, catabolic changes predominating excessively (as the disintegration of axis-cylinder and myelin); and we may be just as certain that a process in which, starting with a mechanical stimulus, we observe a reversion of the adult, resting, neurilemmal nuclei to an embryonic condition, with hyperchromatosis, mitotic activity, nuclear migration, increase of cytoplasm, to say nothing of probable metabolic activity with reference to absorption of dead myelin, is of a regenerative or hyperplastic nature. Certainly in the domain of pathology, where this whole matter has received minute consideration with special reference to the components of the general process of inflammation (see, for example, Ribbert, *op. cit.*, p. 209), no one would think of classifying the fibroblastic proliferative responses as degenerative in character, however markedly retrogressive the general reaction of which they form a part. The concepts of local and general degeneration are not to be confused.

Some of those workers that have maintained the degenerative character of the hyperplasia have apparently been influenced by the consideration that, if the neurilemmal hyperplasia were a regenerative process, the doctrine of peripheral regeneration would be thereby strengthened. But such is by no means the case. The problem—whether the protoplasmic bands have in themselves the inherent property of depositing axis-cylinders—is entirely independent of the hyperplastic character of these bands, and must be settled inductively. Biologically, then, in the light of modern concepts of regenerative and degenerative processes, the proliferation of neurilemma is purely hyperplastic or regenerative.

Nageotte (1915) hints at some special, mutual interdependence of neurilemma and axis-cylinder, but we believe the observations recorded in the present paper show that the sheath is to be regarded as a structure *per se*, independent of any essential genetic relation to the axis-cylinder. In response to mechanical or chemical (toxic) stimuli, it may undergo hyperplasia with reversion to an embryonic state. In so doing, it may and does serve as a conduit for regenerating cylinders. We do not doubt that the latter, under clinical conditions as in certain traumatic nerve injuries, often attempt to push out into ordinary cicatricial tissue, but on leaving the neurilemmal

territory that portion of the fiber usually—perhaps always—succumbs. Probably this is simply a mechanical sequence.⁴

With reference to the mutual relationship between neurilemmal hyperplasia and the closely associated degeneration and absorption of axis-cylinders and myelin there have been many speculations.

It is generally conceded that the granular degeneration of axis-cylinder and of myelin are the earliest of these processes to begin. The death of the axis-cylinder is probably a trophic sequence of isolation from the ganglion cell. Many authors (*e. g.*, Nageotte and Cajal, 1911) hold that the myelin digests the dead axis-cylinders. Of course, numerous observers have shown that fragments of axis-cylinders are enclosed within the "ovoids" or segments of the disintegrating myelin, but no satisfactory proof is as yet available that the myelin digests the dead axis-cylinder. Dr. Bensley, in a recent personal communication, points out that modern concepts of the inherent enzymatic autodigestive powers of all tissues render superfluous such assumptions, except where definite evidence exists. V. Büngner (1891) took a similar conservative position with reference to the disintegration of the myelin which he considers to be a passive process. He also shows that migratory leucocytes have no place in the absorption. Nageotte (1911) states that the chemical products of the degenerating axis-cylinders and myelin furnish the efficient stimulus to the neurilemmal-sheath hyperplasia. Ingebrigtsen (1916) believes that his work confirms Nageotte's idea, for growth of neurilemmal cells in plasma was obtained only when Wallerian degeneration (of axis-cylinders and myelin) had begun in the nerve before its introduction into the plasma. But to insure this, the nerves after section were allowed to remain *in situ* for the four or more days. This, however, introduces a confusing factor, for during those days the neurilemma takes on a very hyperplastic condition. Ingebrigtsen's work, far from showing that the disintegration products of dead axis-cylinders and myelin stimulate the neurilemma to proliferate, indicates that neurilemma, in reverting to this embryonic condition, acquires greatly increased viability and growth potentiality. The fact that the neurilemma, after four days of hyperplasia in the body, grows out into typical protoplasmic bands, morphologically almost identical with those we describe, offers confirmatory evidence as to our conception of the early development of true bands at the traumatized stump.

Moreover, Clark repeatedly obtained marked degrees of degeneration in axis-cylinders and myelin without stimulation of the neurilemmal sheaths to hyperplasia. Also, Ranson proved that protoplasmic bands develop from non-medullated fibers in the distal stump.

There does, however, appear to be evidence that the hyperplastic neurilemmal cytoplasm helps in the absorption of the degenerated myelin and axis-cylinders. Howell and Huber (1892) offered good morphologic proof of this. Clark also

⁴ In this sense the dictum of Bethe may be true: "Die Ganglienzelle allein besitzt überhaupt nicht die Fähigkeit einen neuen Neuriten zu bilden. Damit ein neuer Neurit vorwächst, muss die Ganglienzelle in Verbindung mit Schwann'schen Zellen stehen."

notes that when the neurilemma displayed no reaction, the remnants of axis-cylinders and myelin globules persisted months or over a year unabsorbed, whereas, in the cases in which neurilemmal hyperplasia was produced, they were rapidly absorbed.

Thus, aside from the traumatic factor, which admittedly is of minor importance, we know nothing satisfactory as to the causes of neurilemmal hyperplasia.

MONOGENETIC ORIGIN OF AXIS-CYLINDERS.

It would be superfluous to discuss the enormous literature regarding the doctrine of peripheral regeneration. In general the overwhelming tendency of modern work has been to show that all definitive regeneration of nerve fibers is from the central segment.⁵

Ranson's work offers especially reliable evidence of this. Clark (1914) confirms it also, as regeneration of axones was often complete in his experimental neuritis in the absence of neurilemmal hyperplasia and protoplasmic band formation.⁶

Ingebrigtsen (1913 and 1916) has shown that *in vitro* the axis-cylinders grow only from the ganglion cell or from the central stump of an axone.

On employing this tubulization technique it soon became apparent that we had an excellent opportunity for investigating the possibility of a peripheral regeneration of axis-cylinders. The limits of the present paper prevent the inclusion of details, but, in brief, it is certain that no axis-cylinders appear in the distal segment, until they have grown down in continuity from the central stump, having bridged the gap. The Cajal-Ranson silver method has ensured against confusion of other types of protoplasmic fibrillation with true axis-cylinders.

ORIGIN OF MYELIN SHEATHS.

The limits of this paper forbid our presenting the detailed results of our study of this question by the tubulization method.

We can, however, confirm the general observation of Howell and Huber (1892), of Mott, Halliburton and Edmunds (1904) and of others, that myelin formation proceeds from the distal end of the proximal segment downward. Inasmuch as all these observers approximated their nerve ends, an element of confusion was introduced, as indicated in the conclusion of Halliburton and Edmunds that the myelin formation starts from the point of union of proximal and distal stump and proceeds distally.

We find, as did Stroebe (1893), that the myelin sheath is formed in continuity with the original myelin sheath above, *i. e.*, the first new myelin to appear is that which restores the myelin of the proximal stump that early underwent an ascending degenerative process. Thus it appears at successively more distal levels, and only when the regenerated axis-cylinder has reached the age of about five or six weeks.

Fig. 22 shows a control, the segment removed from a normal nerve at operation—stained with phosphotungstic acid hematoxylin. The myelin sheaths (*a*), shown in white in the microphotograph, are stained a bright blue. The darker areas represent bundles of non-medullated fibers (*b*) and endoneural connective tissue (*c*).

Fig. 23 represents the same nerve seven weeks after operation, the level represented being in the proximal segment about 3 mm. above the plane of section. Some of the medullated fibers are slightly swollen, but the great majority are of normal size or smaller, some not more than one-quarter the diameter of the largest. Note particularly the large bundles of non-medullated fibers (*b*) with closely associated neurilemmal nuclei (*c*). These are, of course, the bundles of regeneration.

Fig. 24 is from the same nerve at the upper part of the regenerated (intermediate) segment. Each bundle is composed largely of non-medullated axis-cylinders (*a*), which do not show in detail in the photograph, but each contains also neurilemmal nuclei (*b*) and fibers which have newly acquired myelin sheaths (*c*). These latter are very delicate, but are stained a bright blue by the Mallory stain and present the usual radiate appearance of the neurokeratin framework.

Fig. 25 shows the same nerve at the lower part of the regenerated (intermediate) segment. Note that the bundles consist entirely of non-medullated fibers with associated neurilemmal nuclei. No medullary sheaths have reached this far distally.

Finally, Fig. 26 again shows the distal stump at 27 weeks, when the bundles of regeneration have long since filled up the old empty canals. Note that even yet a majority of the fibers in each bundle are non-medullated. Those which have acquired medullation seem perfect in morphology. Many neurilemmablasts yet persist, associated closely with the regenerated bundles.

Thus in the nerve shown in Figs. 22 to 25, inclusive, the upper 3 or 4 mm. of the regenerated segment contain at the seventh week of regeneration a considerable number of medullated fibers.

In nerves after nine weeks of regeneration, many of the fibers bridging a gap of 12 mm. have acquired a medullation throughout their extent and even some distance into the distal stump.

Interpretation.—The myelin is laid down *in situ*, whether by activity of axis-cylinder or of neurilemma we could not determine, but undoubtedly it appears only in those portions of the new fiber which have reached an age of about five or five and one-half weeks. All medullated fibers regenerate through the gap as non-medullated ones, which later acquire medullation. All medullation begins proximally and proceeds distally.

Many fibers acquire their medullation much later than the sixth week.

We have no reason to doubt the accuracy of Howell and Huber's observation of the discontinuous appearance of myelin within the protoplasmic bands, but certainly the general progression is from the proximal stump distalwards.

⁵ *Vide* Ranson, 1912, for an excellent review.

⁶ Bethe and other exponents of peripheral regeneration hold that the nerve fibers are laid down within the protoplasmic bands.

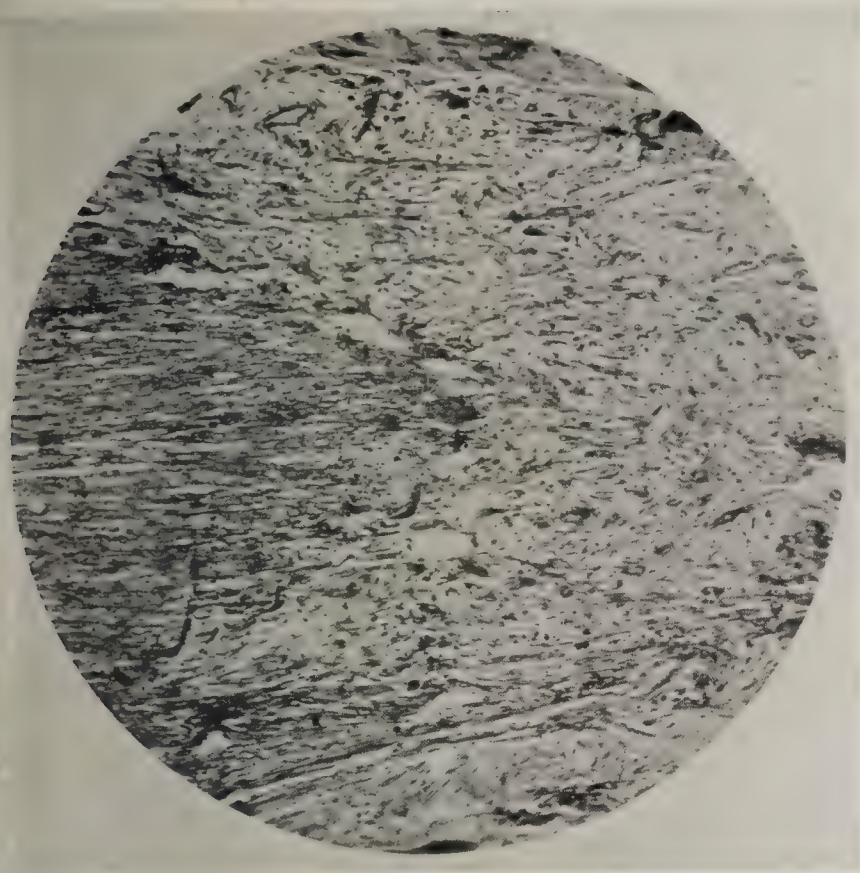


FIG. 4.

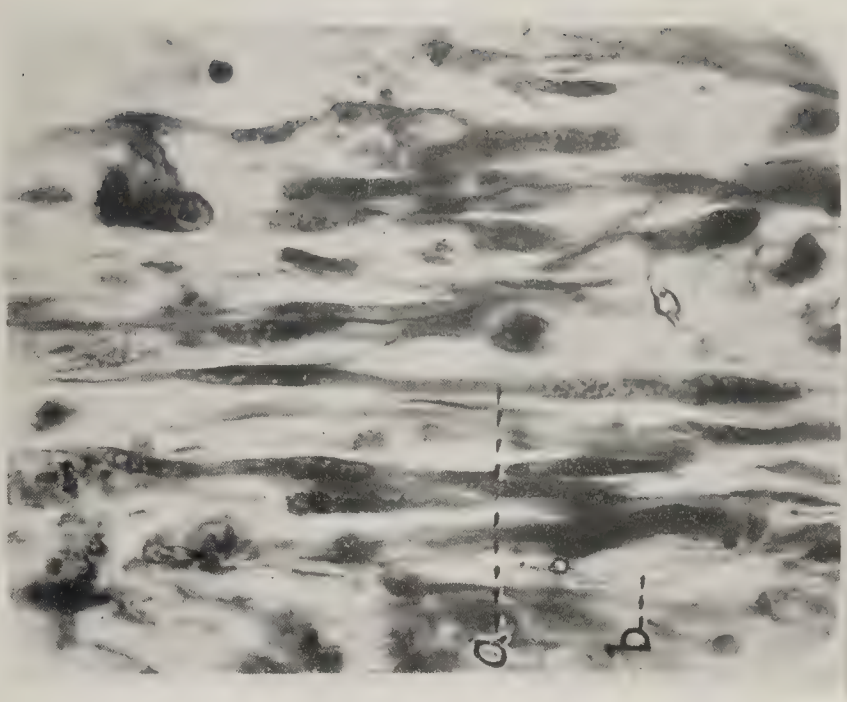


FIG. 5.

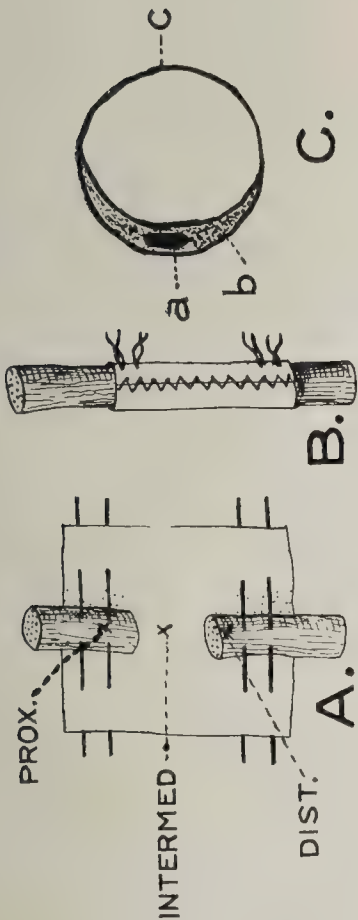


FIG. 1.

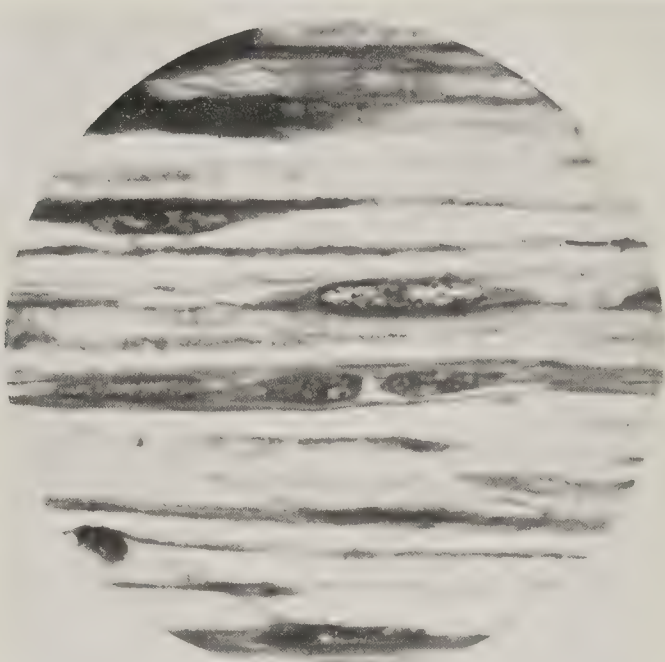


FIG. 3.

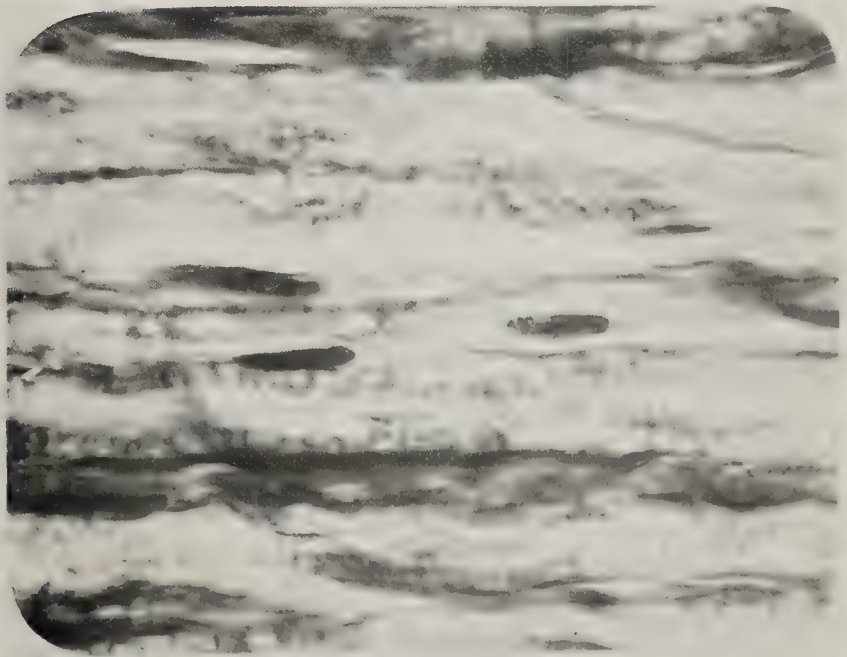


FIG. 2.



FIG. 10.

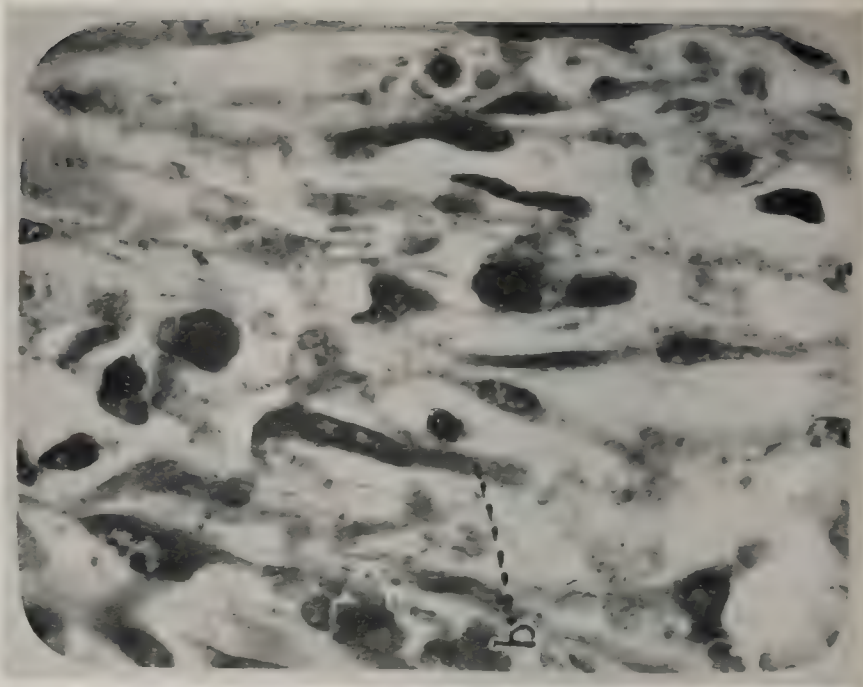


FIG. 9.

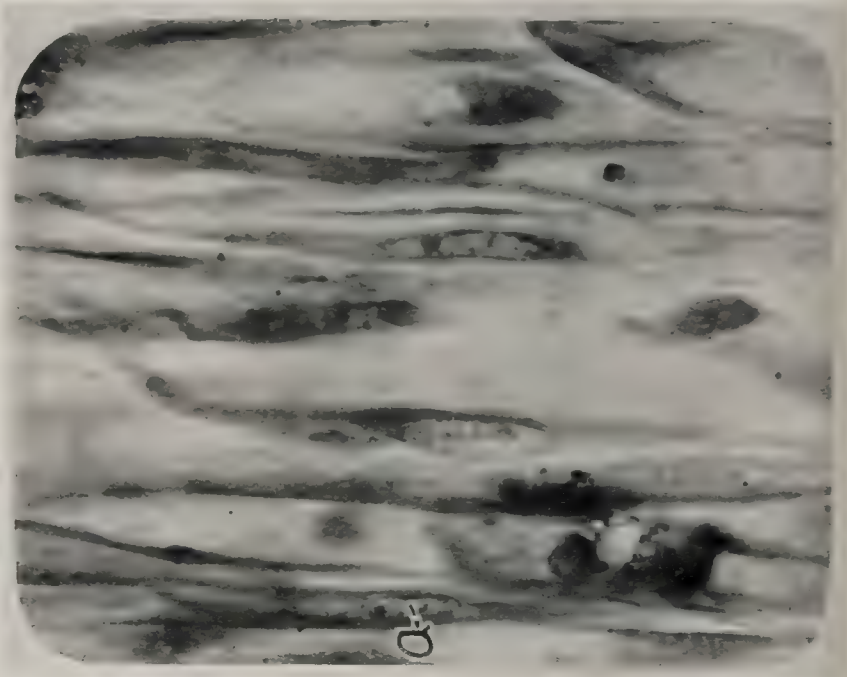


FIG. 8.

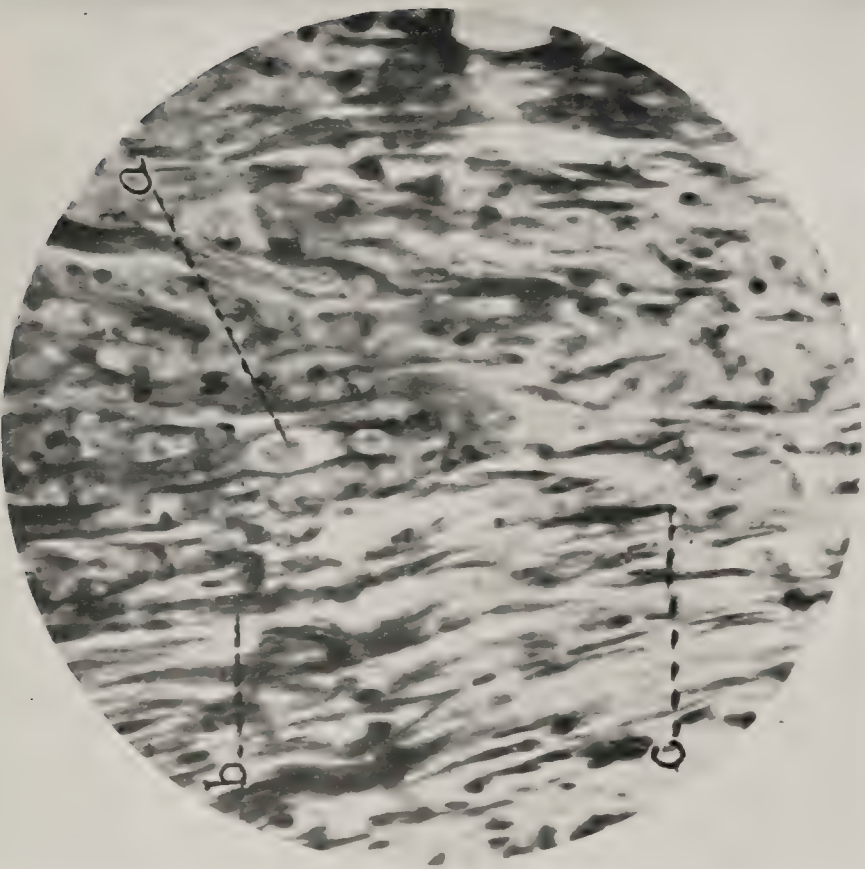


FIG. 6.

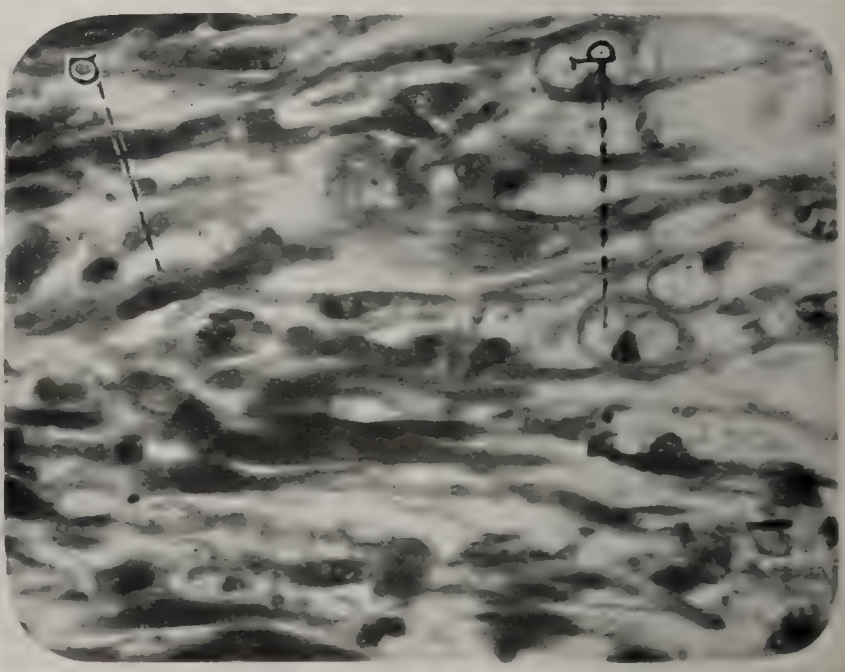


FIG. 7.

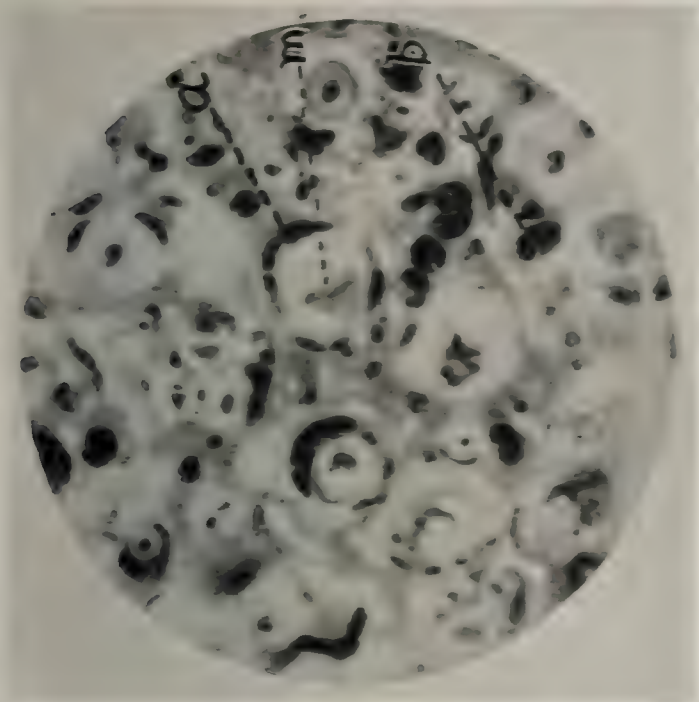


FIG. 15

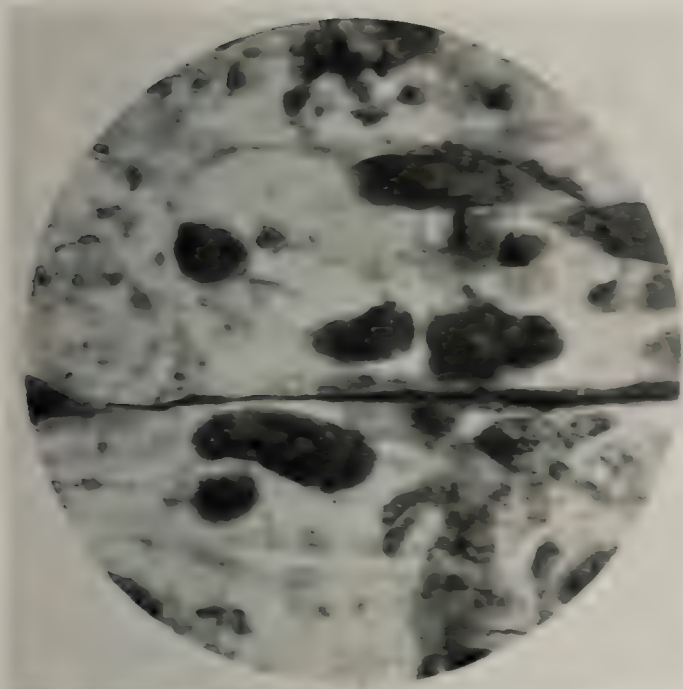


FIG. 12

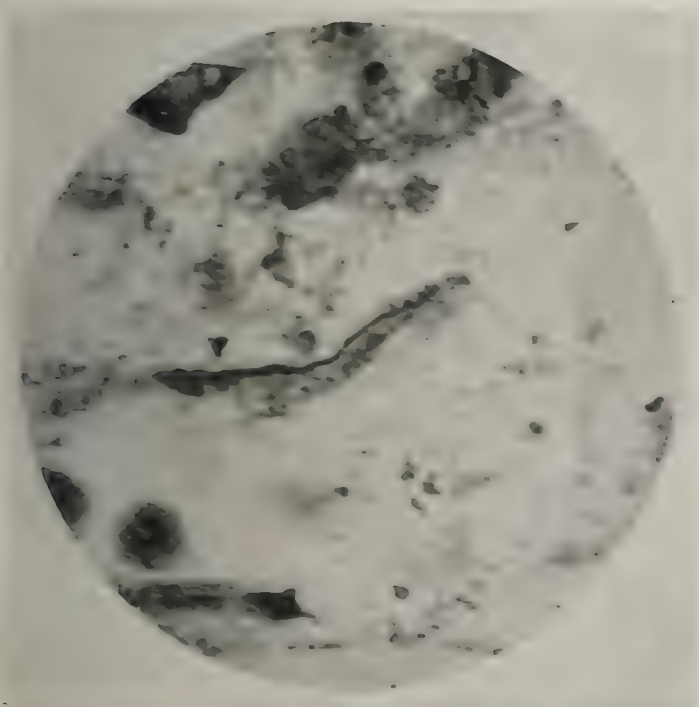


FIG. 11

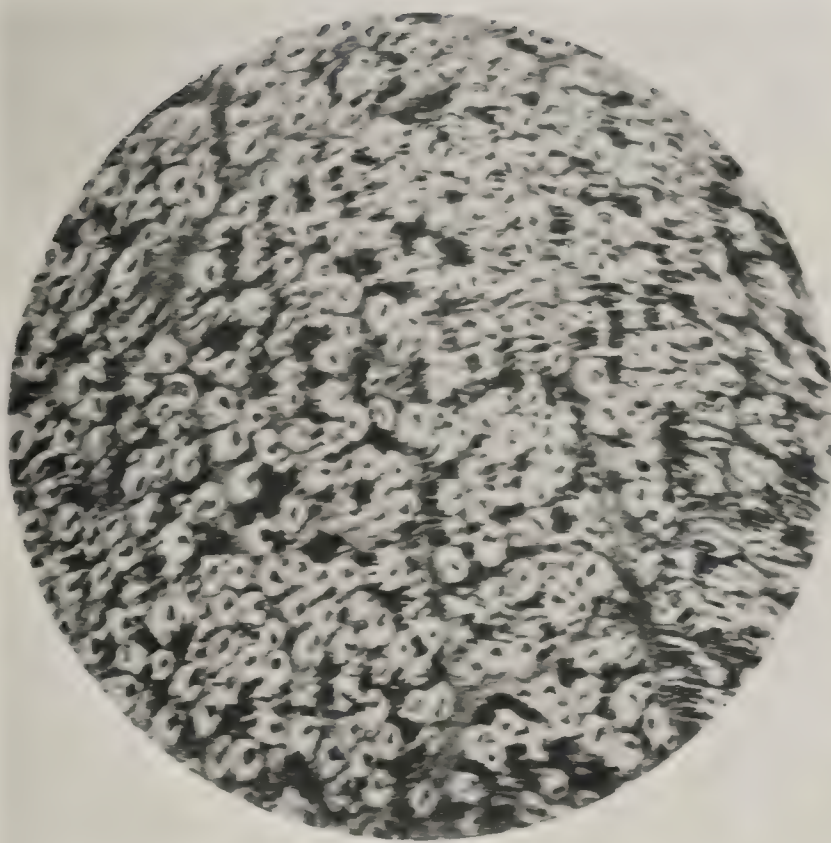


FIG. 14

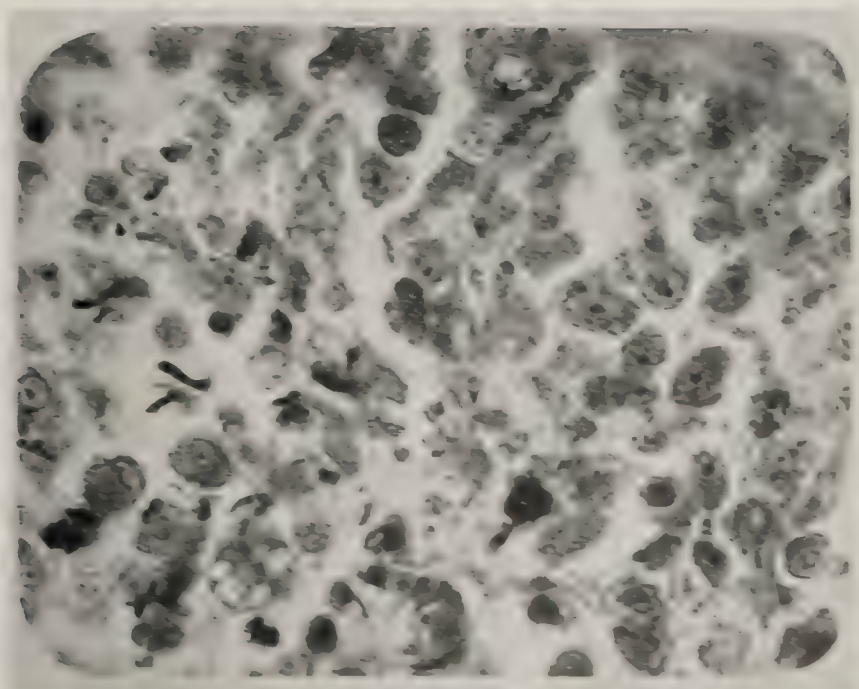


FIG. 13

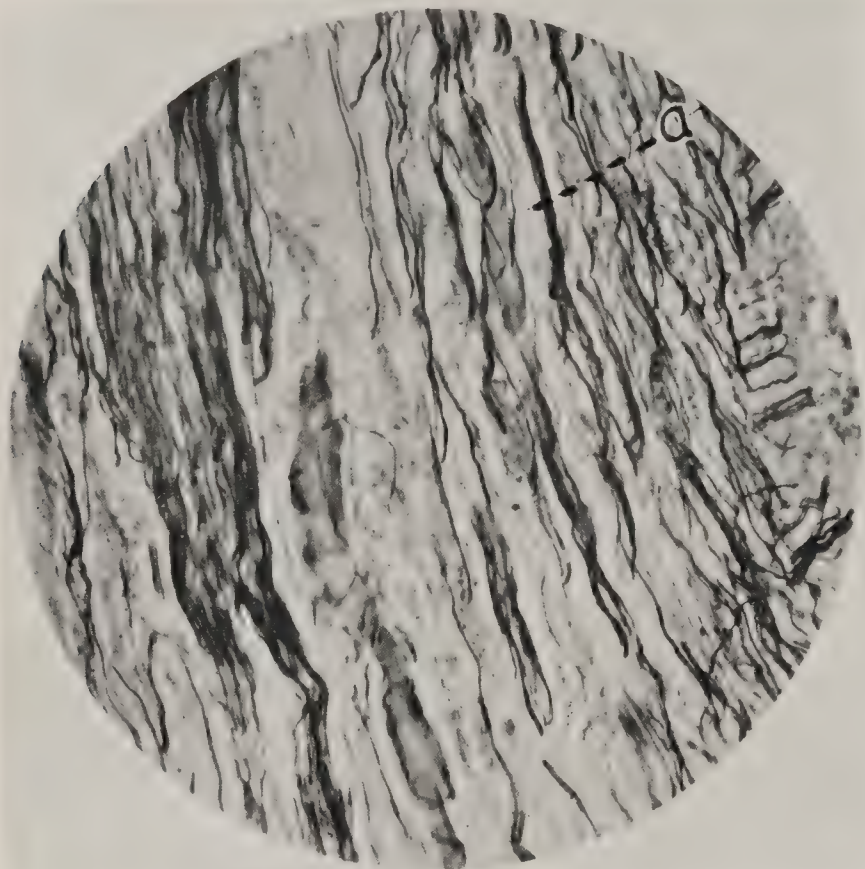


FIG. 16.

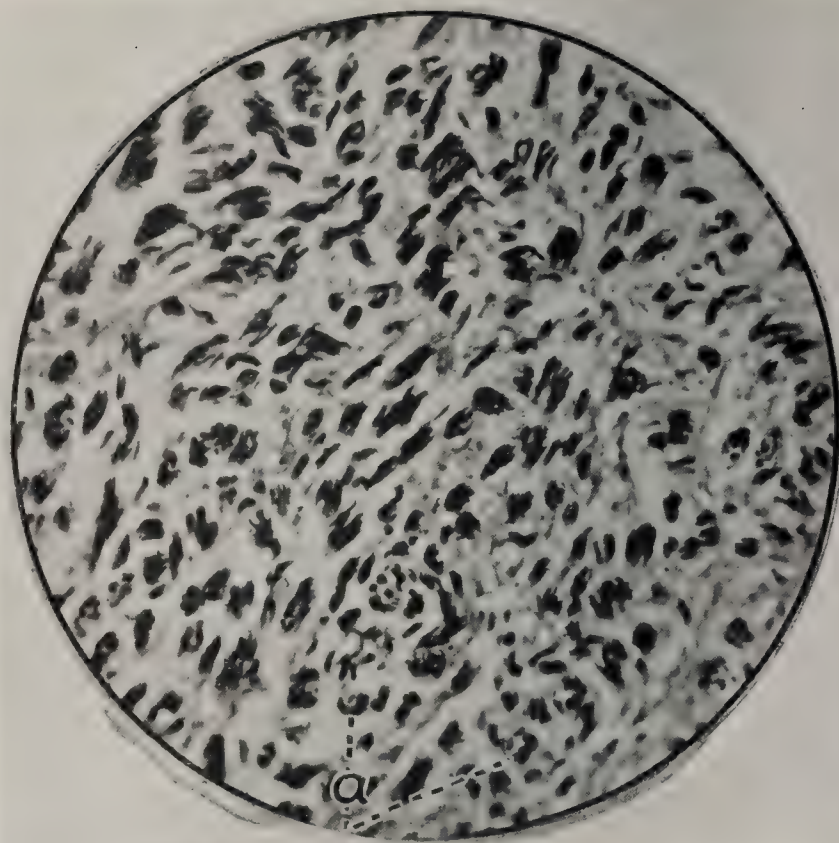


FIG. 17.

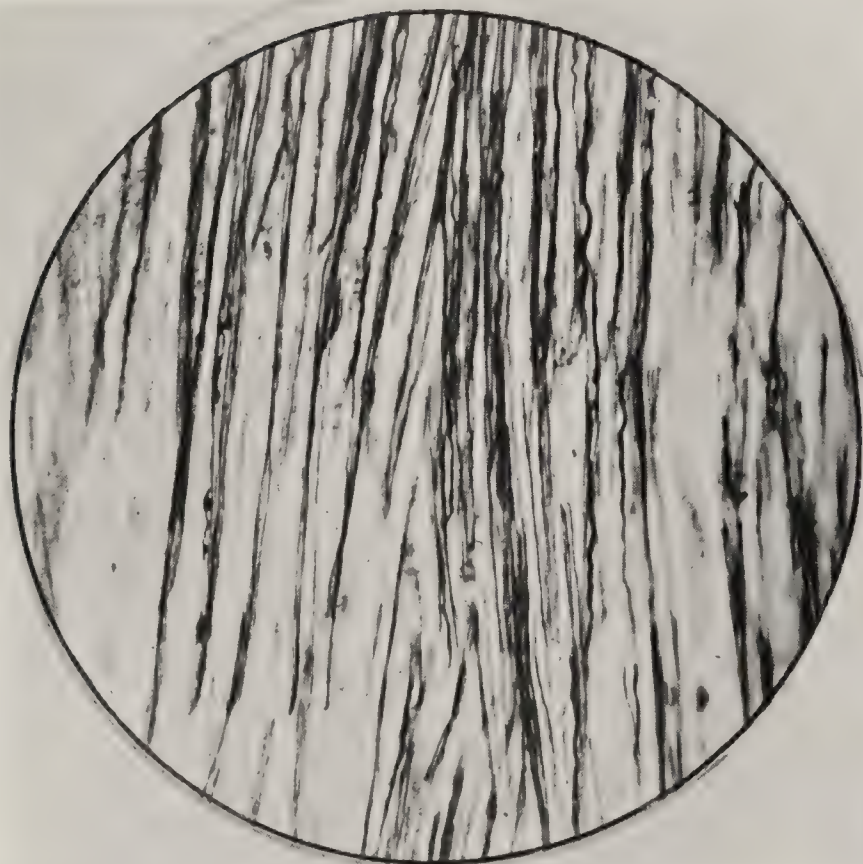


FIG. 18.



FIG. 19.

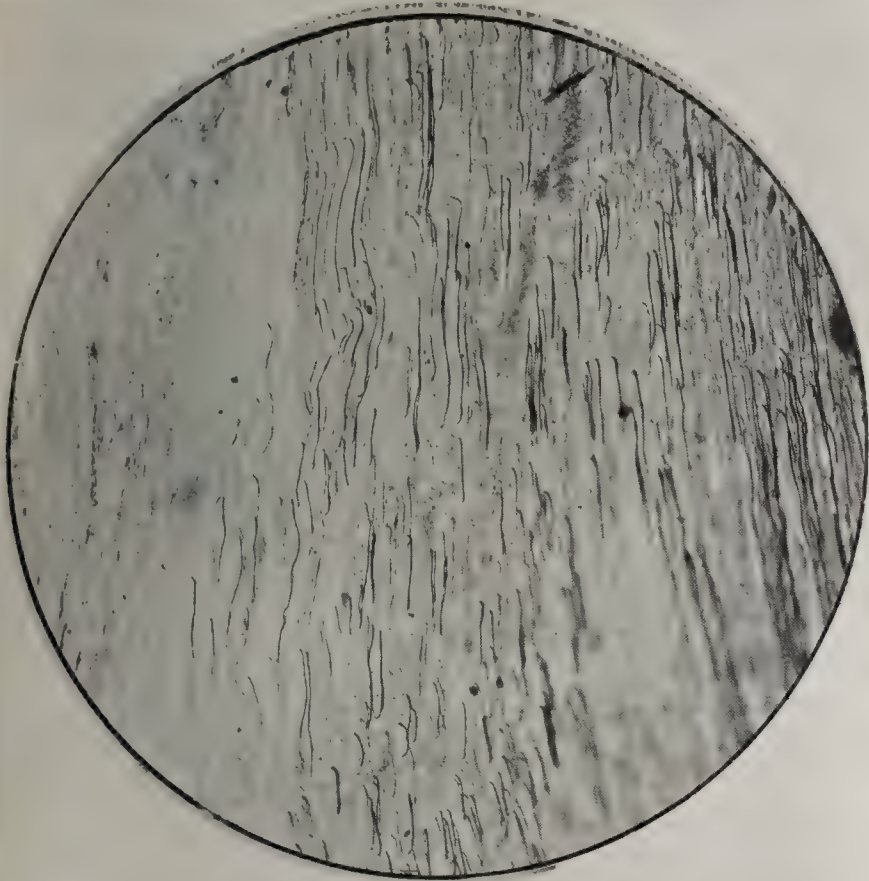


FIG. 20.



FIG. 21.

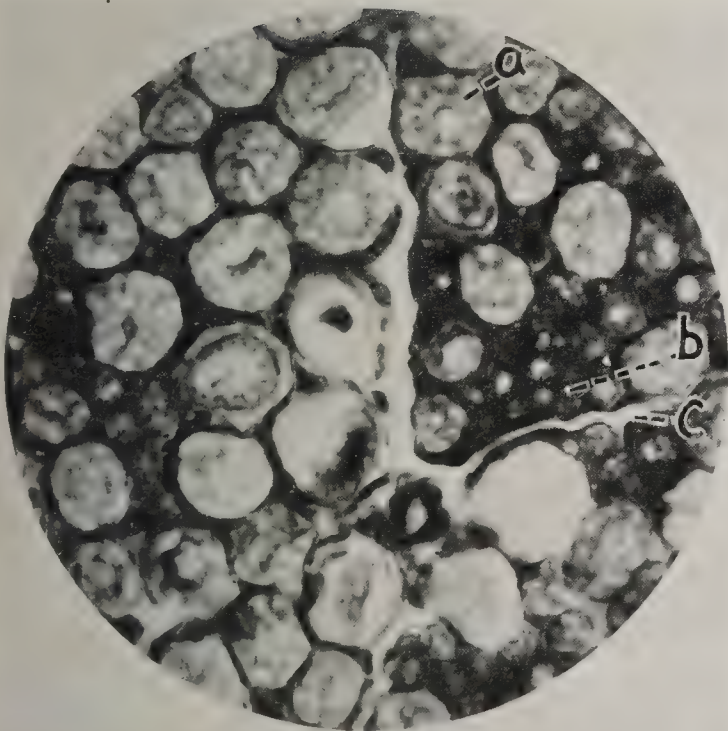


FIG. 22.

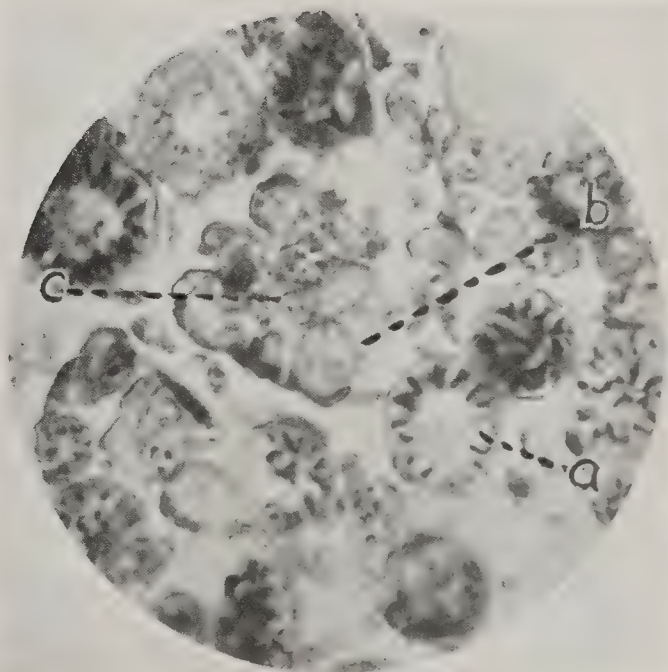


FIG. 23.

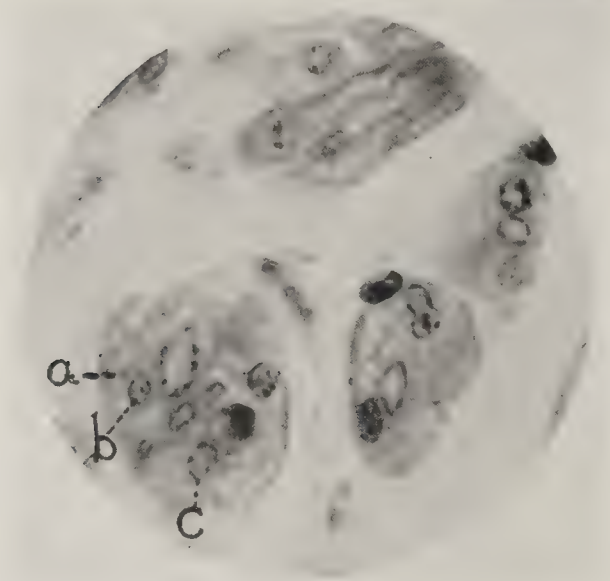


FIG. 24.

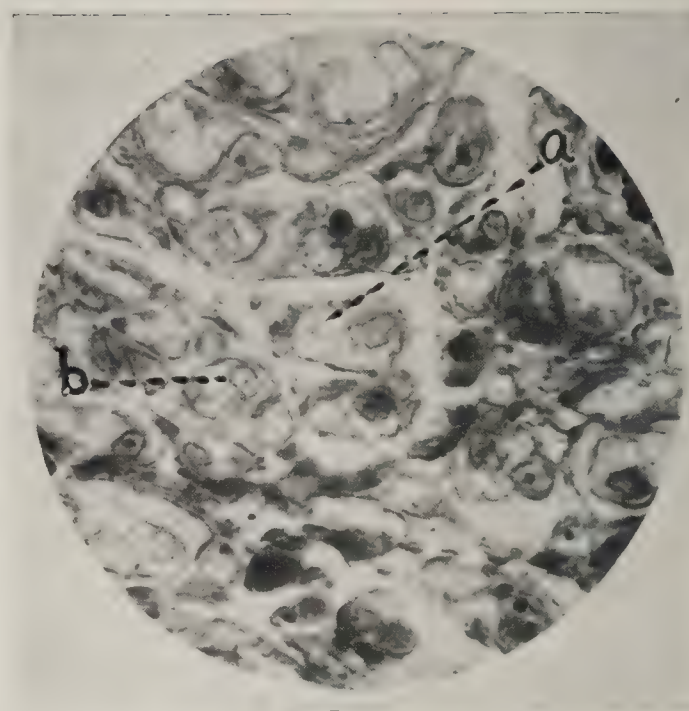


FIG. 25.

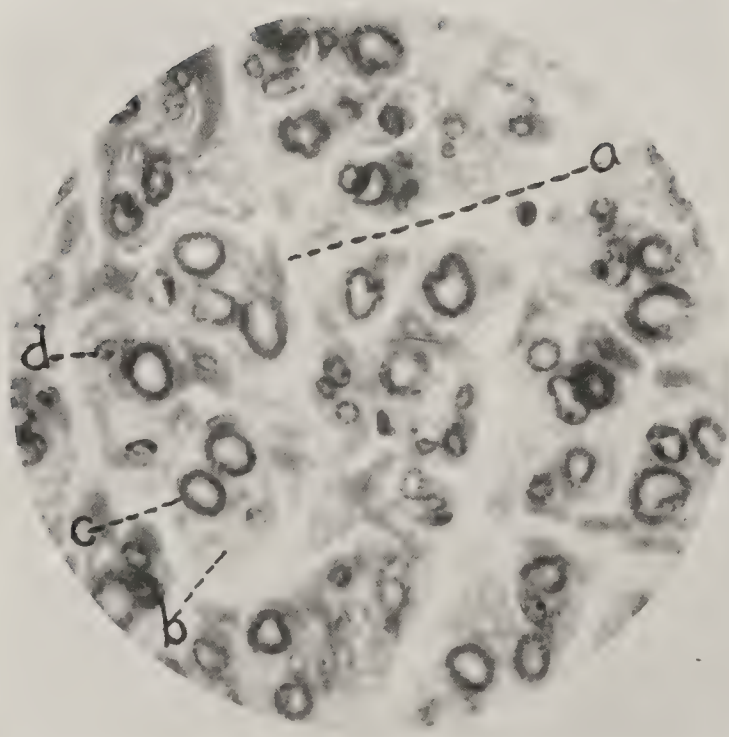


FIG. 26.

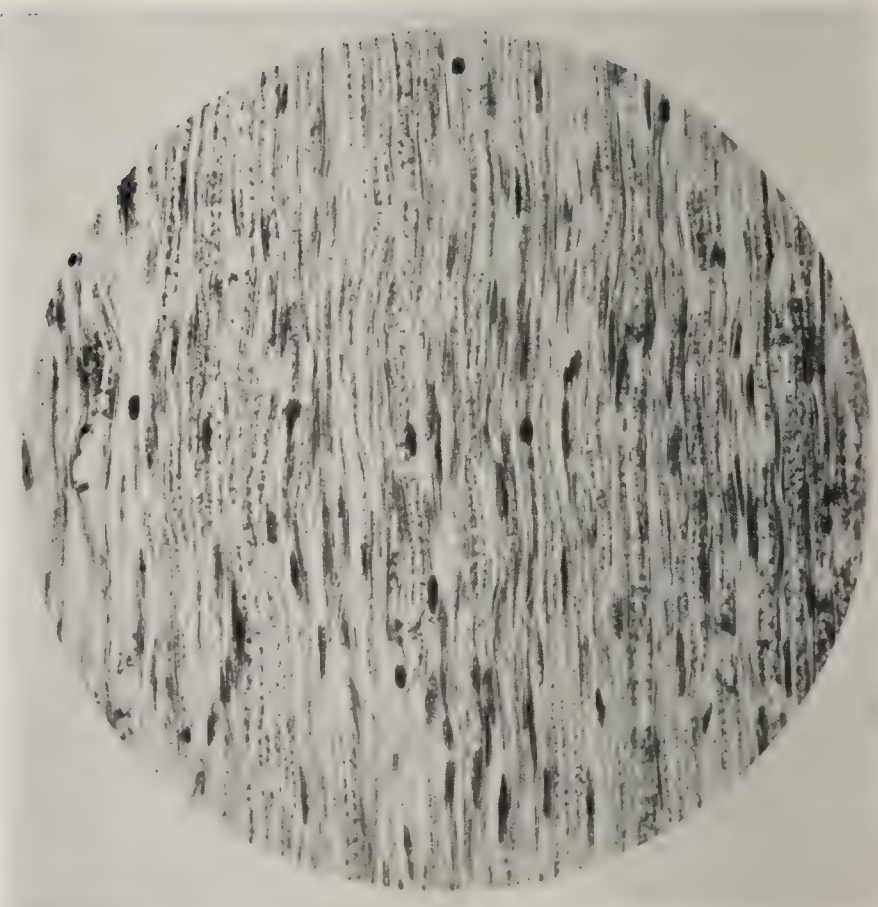


FIG. 27.

SUMMARY.

1. In the immediate vicinity of nerve trauma associated with break of continuity there occurs an accelerated hyperplasia of the neurilemmal elements which results in the early formation of protoplasmic bands. These develop in both proximal and distal stump and tend to bridge the defect. Along these protoplasmic pathways the regenerating axis-cylinders from the central stump pass. Whether they reach the distal stump and neurotise it depends largely on the extent to which these preformed conduits have successfully prepared the way.

2. All efficient regeneration of nerve fibers (axis-cylinders) is from the central stump. All regenerating nerve fibers, whether the outgrowth of medullated or of non-medullated axones, are in their early stages non-medullated.

3. All medullation begins proximally and proceeds distally, appearing only in those parts of the new axis-cylinder which have acquired an age of five or five and one-half weeks (in the dog).

LITERATURE.

- Bethe: Arch. f. d. ges. Physiol., 1907, CXVI, 385.
 Clark: Jour. Comp. Neurol., 1914, XXIV, 61.
 Dustin: Münch. Med. Wchnschr., 1913, LX, 2252.
 Harrison: Anat. Rec., 1908, I, 209.
 Howell and Huber: Jour. Physiol., 1892, XIII, 335.
 Huber: Arch. f. mikr. Anat., 1892, XL, 409.
 Huber: Journal Morphol., 1895, XI, 629.
 Ingebrigtsen: Jour. Exp. Med., 1913, XVII, 182; also, XVIII, 412; also, 1916, XXIII, 251.
 Kirk and Lewis: Jour. A. M. A., 1915, LXV, 486.
 Kirk and Lewis: Anat. Record, 1916 (Jan.), X, No. 3. (Abstract of paper read before Assoc. Amer. Anat., at Yale University, Dec. 28, 1915.)
 Langley and Anderson: Jour. of Physiol., 1904, XXXI, 418.
 Mott, Halliburton and Edmunds: Jour. Physiol., 1904, XXXI. Section on Proceedings, p. 7.
 Nageotte: Compt. rend. Soc. biol., 1911, LXX, 861.
 Nageotte: Compt. rend. Soc. biol., 1915, LXXVIII, 153 and 249.
 Ranson: Jour. Comp. Neurol., 1912, XXII, 487.
 Ribbert: Lehrb. der Allg. Pathologie, 1908.
 Stroebe: Beiträg z. path. Anat., 1893, XIII, 160.

DISCUSSION.

DR. HOWELL: I hardly feel qualified to discuss Dr. Lewis's results, as it has been more than 25 years since I worked upon the subject. At the time when Huber and I were investigating the subject of nerve-regeneration there were still fond hopes that union of severed nerves might take place by first intention with immediate restoration of function. The picture presented by Dr. Lewis of the processes of regeneration is, in most respects, the same as we found and described, except in the matter of the down-growth from the central stump of protoplasmic bands, which precede and guide the development of new fibers. This seems to me a new and interesting observation. The suggestion, quoted from Clark's paper, that the formation of the embryonic fibers is a process of degeneration rather than of regeneration is, I believe, open to criticism. I do not see how you can avoid the conclusion that the regeneration is intimately connected with, and dependent on, the growth and proliferation of the neurilemmal nuclei. The augmented activity of these nuclei is the key-note to the whole process of regeneration. The great rapidity with which they multiply as the old fibers undergo fragmentation

is in fact an extraordinary phenomenon. As Van Gehuchten has pointed out, nothing of this kind is observed in a dead nerve. The underlying conditions which lead to this new growth-activity have not been explained. We may assume as a provisional theory that it is due to some chemical stimulus developed in the process of degeneration of the old fiber or to the formation of specific growth-substances, but so far as I am aware we have no good experimental data in regard to this point.

DESCRIPTION OF FIGURES.

FIG. 1.—(A) Diagram illustrating method of tubulization. (B) Diagram of completed tubulization. (C) Diagrammatic cross-section of hyperplastic neurilemmal sheath: (a) Neurilemmal nucleus; (b) Protoplasmic band; (c) Non-hypertrophied portion of sheath.

FIG. 2.—Control normal nerve. Segment removed at primary operation, illustrating maximal normal number of neurilemmal nuclei. ($\times 1000$.) Phosphotungstic acid hematoxylin.

FIG. 3.—Proximal stump just above plane of section, at sixth day. To illustrate neurilemmal hyperplasia. ($\times 1000$.) Hematoxylin and eosin.

FIG. 4.—Proximal stump, at sixth day. To illustrate down-growth of neurilemmal (protoplasmic) bands into serum of tube. ($\times 75$.) Hematoxylin and eosin.

FIG. 5.—Detail from Fig. 4, showing tip of proximal stump. Note—(a) protoplasmic bands containing neurilemmal nuclei; also (b) degenerated medullated fibers. ($\times 750$.) Hematoxylin and eosin.

FIG. 6.—Distal stump at sixth day. To illustrate proliferation of neurilemmal bands (b) in the nerve tip; also (c) the same growing in serum of tube; and (a) degenerated fragment of axis-cylinder enclosed in a globule of myelin. ($\times 335$.) Hematoxylin and eosin.

FIG. 7.—Detail from Fig. 6, showing tip of distal stump. Note—(a) protoplasmic bands in the serum; also (b) degenerated axis-cylinder and myelin. ($\times 650$.) Hematoxylin and eosin.

FIG. 8.—Detail from distal stump just below level of operative section, at sixth day. Note protoplasmic bands (a). ($\times 1000$.) Hematoxylin and eosin.

FIG. 9.—Detail from a point 10 mm. from proximal, and 2 mm. from distal stump at sixth day. Note protoplasmic bands (b) in serum of tubule; also migratory cells. ($\times 750$.) Hematoxylin and eosin.

FIG. 10.—Detail from growing tip of proximal stump at five and one-half weeks. Note protoplasmic bands with non-medullated axones, the latter stained black. ($\times 1200$.) Silver-pyridine method.

FIG. 11.—Protoplasmic bands containing non-medullated axis-cylinders, the latter stained black, from serum-filled tube just below proximal stump at sixth day. ($\times 1200$.) Silver-pyridine and safranin.

FIG. 12.—Protoplasmic bands with non-medullated axis-cylinder. ($\times 1200$.) Silver-pyridine and safranin.

FIG. 13.—Cross-section at tip of regenerating proximal stump at the eighth day. An area has been selected which shows some protoplasmic bands devoid of axis-cylinders, and some containing them. The latter stain black. ($\times 1000$.) Silver-pyridine.

FIG. 14.—Cross-section of proximal stump, 2.5 cm. above plane of surgical section at sixth week. Note great increase in non-medullated fibers. ($\times 200$.) Silver-pyridine.

FIG. 15.—Cross-section of proximal stump, 3 mm. above plane of surgical section at 31 weeks. Note non-medullated subneurilemmal plexus (a) derived from the medullated axis-cylinder (m) by lateral branching; also bundles (b) of non-medullated fibers, derivatives of a non-medullated axone. ($\times 1000$.) Silver-pyridine.

FIG. 16.—Detail from proximal stump at eight and one-half weeks. Note swollen myelin sheaths (a); also bundles of non-medullated fibers stained black. ($\times 400$.) Silver-pyridine.

FIG. 17.—Cross-section of intermediate segment (*i. e.*, the regenerated hiatus), at sixth week. Note bundles of non-myelinated fibers stained black. Group (a) is derived by down growth from a medullated axone. ($\times 325$.) Silver-pyridine.

FIG. 18.—Detail from intermediate segment at eight and one-half weeks. End bulbs are seen at growing tips of some fibers. ($\times 325$.) Silver-pyridine.

FIG. 19.—Detail from intermediate segment at the tenth week. Note arrangement in bundles. ($\times 200$.) Silver-pyridine.

FIG. 20.—Distal segment at fourth week. To illustrate invasion by regenerating non-myelinated fibers. ($\times 130$.) Silver-pyridine.

FIG. 21.—Distal segment at seventh week. ($\times 70$.) Silver-pyridine.

FIG. 22.—Normal control segment removed from nerve 39 at primary operation. Note (a) myelinated fibers; (b) bundle of non-medullated fibers; (c) connective tissue. ($\times 1000$.) Phosphotungstic acid hematoxylin.

FIG. 23.—Proximal segment of nerve 39 (same nerve as shown in Fig. 22), at seventh week after section. Note (a) medullated

fibers, (b) bundles of non-medullated fibers and (c) neurilemmal nuclei. ($\times 1200$.) Phosphotungstic acid hematoxylin.

FIG. 24.—Same nerve (seventh week). Upper part of intermediate segment (*i. e.*, regenerated hiatus). The bundles consist largely of non-medullated fibers (a) but also contain a few fibers (c) surrounded by delicate myelin sheaths, staining a bright blue and also neurilemmal nuclei (b). ($\times 1200$.) Phosphotungstic acid hematoxylin.

FIG. 25.—Same nerve (seventh week). Lower part of intermediate segment. The bundles consist entirely of non-medullated fibers (a) with neurilemmal nuclei (b). ($\times 1200$.) Phosphotungstic acid hematoxylin.

FIG. 26.—Distal segment at 27 weeks. The bundles consist largely of non-medullated fibers (b) among which are some medullated, (c) and some neurilemmal nuclei (d), which are yet hyperplastic (*i. e.*, neurilemmablasts.) The resting nuclei (a) are probably connective tissue nuclei of the sheath of Henle. ($\times 1000$.) Phosphotungstic acid hematoxylin.

FIG. 27.—Distal segment of a nerve at 31 weeks after operation. To illustrate the persistent hyperplastic condition of the neurilemmal nuclei. ($\times 450$.) Phosphotungstic acid hematoxylin.

THE SIGNIFICANCE OF XANTHOCHROMIA OF THE CEREBRO-SPINAL FLUID.

By T. P. SPRUNT and J. E. WALKER.

(From the Medical Clinics of the City Hospital, Baltimore, and of The Johns Hopkins Hospital.)

In 1903, Froin¹ described in the cerebrospinal fluid from a patient with an organic nervous disease several peculiarities, a yellow color, an increased number of lymphocytes and a marked and rapid coagulation. This condition of the fluid has sometimes been called Froin's syndrome.

Froin² later added other cases and was followed by several of his compatriots, Aubrey,³ Babinski,⁴ Cestan and Ravaut,⁵ Mestrezat,⁶ and others. Considerable interest in this condition has been shown by German writers, as evidenced by many articles in the years from 1909 to 1914 by Schnitzler,⁷ Siemerling,⁸ Klieneberger,⁹ Raven,¹⁰ Oppenheim,¹¹ Nonne,¹² Schlesinger,¹³ and others. More recently in English and especially in American literature we find several references to the subject, notably those by Cooper,¹⁴ Greenfield,¹⁵ Hartman,¹⁶ Kennedy and Elsberg,¹⁷ Collins and Elsberg,¹⁸ Mix,¹⁹ Campbell,²⁰ Horrax,²¹ Bromer,²² Hanes.²³

In different cases there are variations in the amount and rapidity of clot formation, in the presence or absence of lymphocytosis and in the amount of globulin. Owing to the difference in points of view or in methods of examination certain observers in describing what is probably the same type of fluid emphasize some of these characteristics and neglect to mention others. In general the Germans are interested in the large amounts of globulin—the Positive Phase I of Nonne—and frequently say nothing of coagulation, whereas the French lay stress upon the coagulation *en masse* and may make no mention of the presence or absence of globulin or cells. Hence we feel that in tabulating cases for study we should not make the criteria too strict nor attempt to conform too rigidly to the description of any one author, as Mix¹⁹ seems to have done

in insisting upon massive coagulation as a necessary feature of the syndrome.

It is generally recognized that a yellow color may occur in the spinal fluid after a hemorrhage into the ventricles or the subarachnoid space when the cells may have almost or entirely disappeared, and also in purulent or in tuberculous meningitis. In such cases, however, the condition can rarely be confused with the syndrome under discussion, if the other available data are considered.

Practically all authors agree that for the production of this syndrome there is necessary an interruption to the flow of the cerebrospinal fluid, and the formation of a pocket of greater or less extent in which the fluid stagnates and into which various elements pass by transudation from the blood vessels within its walls. Hence one can appreciate the value of such a finding in certain cases of compression of the spinal cord.

The following cases stimulated our interest in this and other types of fluid in compression of the cord, especially the syndrome of Nonne, or, as he speaks of it, Isolated Phase I,²⁴ to which we shall again refer.

CASE 1.—G. A., white, tailor, aged 41, admitted to the City Hospital, June 30, 1915, and discharged June 27, 1916. Med. No. 2950. Tumor of cauda equina. Operation with partial removal; subsequently, treatment with radium; improvement.

The patient complains of "neuritis of both legs." The family and past histories are negative. The present illness began 9 years ago, in 1906, with a sudden pain in the right leg, which increased rapidly in severity and in distribution, extending down the right leg and into the left hip. After an operation on the right sciatic nerve the pain subsided and the patient was able to return to work for 4 years during which there was no trouble

except transient pain in the lumbar region. Five years ago there was another sudden outbreak of pain in both legs which has become progressively worse except for slight remissions. He has been unable to work for 3 years, and unable to walk for 10 weeks. Wasting of the leg muscles began about 3 years ago; occasional retention of urine 2 years ago. There have been numbness and tingling of the feet for several years and a gradual loss of weight of 50 pounds. The pains were so frequent and so severe that the patient got very little sleep.

Physical examination showed an evidently pain-racked, emaciated man, unable to walk, and unable to move in bed without pain and considerable effort. His mentality was clear and the internal organs were not evidently diseased. The spine was held stiffly with practically no flexion or extension, and with only slight lateral motion and very little rotation. The lumbar region was especially rigid and the usual lordosis obliterated. The 12th thoracic and 1st and 2d lumbar spines were a little tender, and there was a more sensitive point just to the left of the 2d lumbar spine. The cranial nerves were normal; the muscular strength in the neck, arms and body was fairly good and the deep reflexes were moderately exaggerated. In the lower extremities there was little complete paralysis, but the muscles were very weak, extraordinarily wasted and flabby and showed numerous fibrillary tremors. There was bilateral foot-drop, complete on the right. The deep reflexes were practically abolished; Babinski's sign was not present in the left foot and there was no response whatever to plantar stimulation of the right. The abdominal and cremasteric skin reflexes were active. No anal reflex was obtainable. The gluteal muscles were atrophic and showed fibrillary twitchings. There was marked impairment of pain, temperature and tactile sensation over the whole of the right foot and the lateral surface of the right leg half way to the knee, and slight impairment above this in front almost to the knee and over the dorsum of the left foot. The deep muscle sense was absent in the right foot. Examinations of the rectum, the stools, the urine and the blood were negative. The X-ray plate of the lumbar spine was negative.

Two lumbar punctures at an interval of about 2 weeks were considered unsatisfactory. Only a few drops of fluid were obtained the first time and less than a cubic centimeter the second time. The fluid was very viscid, of a yellow color and contaminated by fresh blood. It clotted immediately into a jelly-like mass, so that the tube could be inverted without spilling its contents. On the third attempt, 2 cubic centimeters were obtained under very low pressure, the fluid falling from the needle drop by drop. It was perfectly clear, of a lemon yellow color and slightly oily in appearance. Minute globules of an oily substance adhered to the sides of the tube. After about 3 minutes a pale yellow clot began to form and in 5 minutes occupied half the volume of the fluid. The clot had remained unchanged in size 2 days later. The reaction for globulin was strongly positive. With the spectroscope no absorption bands were seen. The Wassermann test of the fluid, as of the blood serum, was negative. Microscopical examination showed no leucocytes, and only 2 or 3 red blood cells in many fields, a few irregularly shaped structureless pieces of material, and many globules of varying sizes, very highly refractile, which stained intensely with Sudan III. With the polarizing microscope, many of these globules were definitely doubly refractile.

The diagnosis was made of an intradural, extramedullary tumor involving the roots of the cauda equina, and on Sept. 28, laminectomy was done by Dr. Arthur M. Shipley. A very vascular, soft, purplish mass was found covering the cauda and extending along the nerve roots. At a second operation, one week later, much of the very friable tumor mass was removed, but a large part of it necessarily remained. Microscopic study showed that the tumor was a glioma. Convalescence from the operations was satisfactory and the patient's pain was greatly ameliorated, although

very little objective improvement was manifest for several months. By April, there were definite evidences of improvement; the area of anæsthesia had become a little smaller, some power of voluntary movement had returned in the toes of the right foot and the patient was able to walk a little with assistance.

In May and again in June, 1916, through the courtesy of Dr. Burnam, he was treated with radium over the lumbar spine. At the time of his discharge, the patient had no pain; he was able to walk with the help of crutches, and had gained many pounds in weight. There were still a few fibrillary twitchings in certain muscles, tenderness over the tumor site and almost complete paralysis and anæsthesia of the right foot. Reports 2 months and 3 months after discharge were encouraging.

CASE 2.—W. H., white, student, aged 15, admitted to The Johns Hopkins Hospital, Oct. 23, 1914; discharged Nov. 23, 1914. Medical No. 33225. Multiple sarcomata of the spinal cord; exploratory laminectomy; death 2 months after discharge from hospital.

The patient complains of nervousness. His family and past histories are negative. The present illness began 6 months before with an injury to his right shoulder and chest, which was not considered serious. Ten days later pain began in the upper portion of the right chest; later it extended downward and appeared also in the left scapular region. Six weeks ago the left leg became numb, and this was followed after 2 weeks by similar sensations in the right leg. During the past 3 weeks, there has been weakness in the legs, marked nervousness and stiff neck. The pain disappeared.

Physical examination showed a fairly well nourished boy and, other than neurological, was negative. There was slight nystagmus and a slight tremor of the tongue. The eye-grounds were negative. There was no limitation of movement in the cervical, thoracic or lumbar regions of the spine and no tenderness over the spine. A jaw-jerk was present and the deep reflexes in the arms were exaggerated. The abdominal skin reflex was absent except in the left lower quadrant. Weakness in the leg muscles, especially on the right, was evident with definite hypertonicity but no atrophy. The gait was spastic, the knee-jerks were greatly exaggerated, with a well sustained ankle and patellar clonus on both sides and bilateral positive Babinski and Oppenheim phenomena. There was definite hypæsthesia below the level corresponding to the 3d thoracic segment, but no hyperæsthesia or absolute anæsthesia. There was no sphincter disturbance.

Examinations of blood, urine and stools were negative. X-ray plates of the cervical, thoracic and lumbar spine were negative.

Lumbar puncture: Ten cubic centimeters of perfectly clear, yellow, straw-colored fluid were obtained under a pressure at first of 100 mm. It clotted completely on standing so that the test-tube could be inverted without spilling the fluid. Before clotting, there were 61 cells per cubic millimeter, all mononuclears. The Ross-Jones test was strongly positive. The guaiac reaction and spectroscopic examination were negative. The Wassermann tests of fluid and blood serum were negative.

Diagnosis. Compression of spinal cord in upper thoracic region, probably by a tumor. An exploratory laminectomy, by Dr. Heuer, of the first four thoracic vertebræ, revealed a very vascular dura. When it was opened, the arachnoid did not bulge as a distinct layer, as is usual, but was evidently filled with the tumor, to which it was quite adherent everywhere. When the arachnoid was pricked, there was only a trace of fluid, and neither above nor below could fluid be encountered. Four distinct tumor masses were seen on the dorsal surface of the cord, one at the highest exposed portion extending across the cord. The remaining tumors almost filled the space to the lower limit of the exposure. One of them, the size of a hickory-nut, which was attached by a small pedicle, was removed for microscopical examination. The tumors had a glossy, friable appearance and were evidently sarcomata.

The microscope showed a very cellular, quite vascular tumor with little stroma. The cells were round or pear-shaped with many mitotic figures—the typical picture of a round-cell sarcoma.

After the operation sphincter control was lost, but was regained after a few days. Catheterization became necessary. Decubitus ulcers began to develop. The patient left the hospital in the ambulance and died 2 months later, completely paralyzed from the neck downward.

CASE 3.—A. G., white, Pole, aged 41. Admitted to the City Hospital, Oct. 5, 1915, and died Nov. 9, 1915. Retroperitoneal metastasis from malignant tumor of the testis; extension through the lumbar and thoracic vertebræ; compression of spinal cord; autopsy.

The patient complained of pain in the leg and back. Three years before admission, there had occurred a slight injury to the left testis which soon began to increase a little in size. One year before admission the rate of growth became more rapid until, in Nov., 1914, there was a tumor as large as a cantaloupe. This was removed in the Urological Department of The Johns Hopkins Hospital. There had been a loss of 50 pounds in weight.

(On investigation, it was learned that retroperitoneal metastases had been recognized at the time of operation and had been considered too extensive to justify a radical procedure.)

The present illness had begun in the summer of 1914 with pain in the lumbar region. This had become worse after the operation, and had soon appeared in the left leg, and after several weeks in the right leg also. The legs had then become progressively weaker and for 3 weeks before admission the patient had been quite unable to walk. Paræsthesias in both legs, slight swelling of the feet, some sphincter disturbance and loss of libido and potentia had been noted for several weeks.

Physical examination showed an emaciated man evidently in considerable pain, which was increased on any attempt to move. The patient lay constantly in a semi-recumbent position which made examination of the abdomen somewhat difficult. There was fairly marked rigidity of the abdominal muscles, slight diffuse tenderness and a hard, palpable mass in the left hypochondrium. This mass caused a bulging of the lower thoracic wall on the left side which was especially well seen in the back. There was both scoliosis and kyphosis of the lumbar spine with the convexity to the left and the apex at the 2d lumbar spine. There was also a definite gibbus, of which the second lumbar spine formed the most prominent point. Tenderness over the 1st, 2d and 3d lumbar spines was present.

The left testicle was missing and near the operative scar in the left inguinal region there was a small nodule about the size of an olive.

Bilateral foot-drop was evident; very little voluntary movement was possible in the left leg, and the right leg was very weak. Atrophy was not marked and there were no fibrillary tremors. The knee-jerk was absent on the left, very sluggish on the right; ankle-jerks were not elicited. There was no response to plantar stimulation. The abdominal, cremasteric and anal reflexes and the deep reflexes of the upper extremities were present and equal. There was marked impairment of epicritic sensation over the dorsum of both feet and a zone of hyperæsthesia pointing to the 12th thoracic segment.

Lumbar puncture. The fluid was under very low pressure: Four cubic centimeters were obtained, of a pale yellow color. A thin web-like clot formed after standing for 12 hours; the globulin reactions were strongly positive; the guaiac and spectroscopic tests were negative. Microscopically, there were 3 lymphocytes to the cubic millimeter. There were many doubly refractile droplets staining with Sudan III.

Three weeks later, when the symptoms of compression were much further advanced, another puncture was done. This fluid was water clear, under very low pressure, and contained 12 cells

per cmm. The Ross-Jones and Pandey reactions were faintly positive. No droplets were found like those seen in the first specimen, nor were any abnormal cells discovered.

The blood, urine and stools were not significantly abnormal; phthalein excretion 42% in 2 hours; Calmette 1% negative; Wassermann negative. During the month in the hospital, the mass increased rapidly in size; the edema of the legs increased, fluid collected in the knee-joints and in the abdominal wall; the paralysis of the legs became complete and 3 weeks after admission the whole body below the level of the xiphoid was completely anæsthetic. One week later, the anæsthesia reached the level of the nipples. The temperature was irregularly intermittent, often reaching 103° F. Death occurred on Nov. 9, 1915.

Autopsy No. 652. Anatomical diagnosis. Primary: Operation, removal of malignant tumor of testis: metastasis to retroperitoneal lymph nodes with extension to bodies of lumbar and lower thoracic vertebræ; extension into spinal canal with compression of cord; infiltration of nerve roots of cauda equina; invasion of left renal pelvis; hydronephrosis and atrophy; extension into vena cava with propagated thrombus distal to tumor mass; compression of abdominal aorta.

Subsidiary: Chronic bronchitis; organizing bronchopneumonia; decubitus ulcer.

CASE 4.—G. H., white man, age 57, admitted to the City Hospital, Sept. 6, 1916; transferred to the Surgical Service Sept. 8; died Oct. 9, 1916. Fracture of spine in lower thoracic region with marked displacement: flaccid paraplegia.

The patient complained of "loss of the use of the body below the pit of the stomach." The family and past histories were negative. The present illness had begun with a fall from a wagon 8 days before admission. He had fallen on his back, and could not get up, had soon become unconscious and had been carried to his home. Examination showed a well nourished man in no acute pain. The abdomen was symmetrical, with distended, tortuous veins on the left side, tenderness on pressure in both upper quadrants, a palpable liver and a distended bladder. There was a sharp kyphosis at the level of the 12th thoracic vertebra with a correspondingly marked depression just below this point. The cervical and dorsal vertebræ showed perfect alignment, and from the 2d lumbar downward the vertebræ had preserved their normal interrelationships. The axes of the two portions, however, were not the same; the upper end of the lumbosacral portion was displaced markedly to the right. There was incontinence of urine and feces; the lower extremities were completely paralyzed with absence of deep reflexes, no response to plantar stimulation, and complete anæsthesia below the level corresponding to the 9th thoracic segment.

Lumbar puncture between the 3d and 4th lumbar spines gave a clear, amber fluid under somewhat decreased pressure. The globulin reactions were very strongly positive: there was no coagulation. The guaiac reaction was positive and the spectroscopy showed the absorption bands of oxyhemoglobin. There were no red blood cells, but 16 mononuclears per cubic millimeter. The Wassermann tests on the blood serum and fluid were negative.

The patient lived for several weeks and died Oct. 9, 1915. At autopsy, the only significant lesions were fracture of the 11th thoracic vertebra with marked displacement and complete destruction of the spinal cord at this level.

We have reported in some detail 4 cases that showed the so-called Froin's syndrome in the cerebrospinal fluid, 2 cases of neoplasm of the cord or its membranes, 1 of a secondary tumor involving the vertebræ and spinal canal, and 1 of traumatic fracture of the vertebral column with displacement in the lower thoracic region. The duration of disease in the

different cases varied greatly, 9 years in 1, 1 year in another, 6 months in another and 1 month in the last case.

The fluids were essentially similar with minor variations, and were characterized particularly by clear transparency, yellow color, strong globulin reactions and low pressure. Spontaneous coagulation occurred in all except Case 4, either immediately or after standing a short while. There was an increased cell count in Case 2, but in none of the others. Case 4 was complicated by the hemorrhage which necessarily occurred with so much displacement of the vertebræ and the consequent laceration of the cord and its meninges, but in the other 3 cases tests for hemoglobin derivatives were negative. The occurrence of the doubly refractile droplets of myelin seems to be very unusual. The only similar observations of which we know are those of Krönig,²⁵ who found myelin droplets and larger fragments of tissue in the fluid from cases with areas of cerebral softening that had ruptured into the subarachnoid space. Degenerating tumor cells have been described a number of times and cholesterol crystals²⁶ at least once. The oily character of the fluid in our first case was evident on gross inspection and the droplets formed a striking part of the microscopic picture. Tumor cells were observed in none of our cases.

It cannot be said that the character of the fluid was a necessary factor in the diagnosis of any of our cases. But, as a matter of fact, our first patient had been set aside as the victim of a system disease, for which little could be done; and it was the unusual spinal fluid which reawakened our interest and led to the correct diagnosis, which should have been made without the assistance of the fluid.

The 4 cases show well the anatomical basis for the formation of such fluids as well as some of the different pathological processes by which it may be brought about. In 2 cases, there were intradural extramedullary tumors which completely filled the subarachnoid space and effectually shut off the spinal fluid below the lesion. In Case 3, a metastatic extradural tumor brought about the same result, and in the fourth instance the fracture with very marked lateral displacement in the lower thoracic region severed all communication between the two portions of the subarachnoid space. In addition, the presence of vascular tumors within the dura in 2 cases doubtless facilitated exchanges between intravascular and subarachnoid fluids. In the traumatic case, dissolved hemoglobin doubtless contributed to the color of the fluid and, in our opinion, accounted for its darker tint. The globulin, however, was increased to a much greater extent than the amount of blood alone would explain.

In our review of some 100 cases from the literature we find that almost all that have been sufficiently studied anatomically at operation or autopsy have shown this obstruction in the subarachnoid space. Tuberculous spondylitis,^{7 10 22} intradural tuberculous granuloma,²³ extensive adhesions between cord, arachnoid and dura in cases of meningo-myelitis,⁶ and gumma of the meninges,¹² are some of the other lesions responsible for such obstructions. Mestrezat⁶ insists that the main determi-

nants are the isolation of the lumbar cul-de-sac and vascular alterations within its walls.

There are some exceptions which are difficult or impossible to explain on the basis of compression and obstruction, but they usually show variations from the complete syndrome in the absence of spontaneous coagulation or of increased globulin or of both. A brief discussion of these cases follows:

1. Siemerling's⁸ case of gliosis spinalis with syringomyelia is an apparent rather than a real exception, since the gliosis in the cervical region was really an intramedullary tumor of unusual dimensions and probably large enough to obstruct the subarachnoid space.

2. Schnitzler's⁷ case of myelitis funicularis is more difficult to understand. At autopsy, besides the myelitis, only a deep scar was found in the lumbar region, the cause of which was not determined. The fluid was described as in small quantity, and intense lemon yellow in color; globulin was present, the lymphocytes were increased, but there was no coagulation, and tests for blood were negative.

3. Kennedy and Elsberg¹⁷ describe a fluid "of light yellow color; globulin present, lymphocytes increased, 20 cells to the cubic millimeter" in one of their 5 cases of a peculiar disease of the cauda equina, in which the nerve roots were swollen, congested and a bluish-red color. They make no mention of coagulation or of tests for hemoglobin derivatives. This should probably be included among the cases in our fifth exception.

4. Three cases^{1 10} are described as clinically resembling Landry's paralysis. One²⁷ of the patients recovered after 3 months. No autopsies were held in the other cases.

5. Finally there is a larger group of 8 or 9 cases,^{21 28} usually of brain tumors in contact with the meninges or ependyma of the ventricles, in which the yellow color and other abnormalities in the fluid may be explained by repeated, small hemorrhages into the subarachnoid space. Spontaneous coagulation is usually lacking, the globulin is small in amount, the pressure is normal or increased, and there are crenated red blood cells or positive tests for hemoglobin. Such fluids may be perfectly clear or slightly turbid. These features with the clinical data usually distinguish such cases sufficiently. This type of fluid is probably more common than the number of published reports would indicate.

As examples of this type, the following cases are reported briefly:

CASE 5.—K. N., white woman, age 37, admitted to City Hospital, March 23, 1916; discharged April 1, 1916; admitted to the University of Maryland Hospital, Sept. 8, 1916, and died Oct. 5, 1916. Autopsy. Endothelioma of dura, left middle fossa.

The patient complained of severe headaches on the left side of the head and face which had been present for a year and were becoming more frequent and more severe.

The general physical examination was negative except for emaciation. The eye-grounds and paranasal sinuses were normal. On neurological examination, there was found paresis of the left abducens, causing an internal strabismus. The left visual field was slightly smaller than the right, and there was interlacing of the color fields. The deep reflexes were slightly increased. The Wassermann test for the blood serum was negative and the spinal

fluid was normal. The urine and blood pressure were normal. There was a slight secondary anæmia.

The patient left the hospital unimproved and came under observation again at the University Hospital on Sept. 8. Her general condition was worse, the headaches were constant, the abducens paralysis was complete. The veins of the left retina were somewhat larger and more tortuous than those of the right. Examination of the other cranial nerves was not altogether satisfactory owing to the patient's lack of coöperation. No other definite abnormalities were discovered and the general examination revealed nothing significant.

On lumbar puncture soon after admission, the cerebrospinal fluid was clear, of a light lemon color, under normal pressure, did not clot, gave negative globulin tests and contained 4 cells per cubic millimeter. The Wassermann test was negative, as it was repeatedly in the blood serum.

A second puncture, one week later, showed a fluid of faint yellowish tinge, clear, with a very faintly positive globulin test. It did not clot. Microscopically there were a few, old crenated red blood cells, but the guaiac reaction was negative.

At a third puncture the fluid was normal.

The patient died on Oct. 5, 1916.

At autopsy, the only significant lesion was a dural endothelioma at the base of the brain in the left middle cranial fossa.

We are indebted to Dr. Gordon Wilson for the privilege of using the records from the University Hospital.

Dr. W. T. Longscope sent us full records of the following case which was observed in his service at the Presbyterian Hospital, New York, and which through his courtesy we report in abstract:

CASE 6.—B. G., woman, age 43, admitted to the Presbyterian Hospital, N. Y., Feb. 14, 1913. Died March 7, 1913. Autopsy. Arteriosclerosis, chronic diffuse nephritis, arterial hypertension, hemorrhages into the lateral ventricles.

The history was a typical one for a case of this type. The patient had been treated several times during the preceding 7 years for similar attacks.

Two months before admission she "took cold," had severe headaches, prostration, dyspnoea, anorexia and vomiting. The chief complaint was of headache.

On examination, the patient was a large woman with moderate dyspnoea; slight cyanosis; large, thick-walled peripheral arteries; blood pressure 210 mm. systolic and 140 diastolic; neurorinitis; urine of small quantity, high specific gravity, a trace of albumin, a few R. B. C., no casts, moderately reduced phthalein. The intense headaches persisted in spite of venesections, hot packs and sodium nitrite.

On Feb. 22, a lumbar puncture with removal of 20 cc. gave much relief from headache.

The fluid was clear, yellow, did not coagulate, gave a positive globulin test and faint blood reaction. The Wassermann was negative. There were 2 cells per cubic millimeter.

On Feb. 26, the spinal fluid was again yellow with a marked blood reaction by the guaiac test but no absorption bands in the spectrum.

After 9 days of comparative comfort, sudden coma occurred with muscular twitching and stertorous breathing, and flaccid paralysis of the left arm and leg.

By phlebotomy, 300 cc. of blood were removed, on which the following chemical determinations were made: urea, 0.020; NaCl, 0.97; sugar, 0.295%. The urine from this period was 140 cc. in quantity and contained 0.6% sugar or 0.84 grams.

Lumbar puncture gave 15 cc. of freshly bloody spinal fluid under some pressure.

Death occurred about 12 hours after the onset of coma.

Autopsy diagnosis: Chronic diffuse nephritis (early arteriosclerotic kidney); cardiac hypertrophy; chronic interstitial myocarditis (early); cerebral hemorrhage into right ventricle, fresh; cerebral hemorrhage into left ventricle, old; pulmonary edema; bronchopneumonia (early); chronic interstitial pancreatitis (focal sclerosis with involvement of Islands of Langerhans); chronic passive congestion of viscera; fibromyoma of uterus; cystic ovary.

In regard to the source of the xanthochromia, we do not consider it necessary to presuppose minute hemorrhages into the meninges and subarachnoid space to explain the coloration of fluids in which no red cells can be found, in which the most delicate chemical tests for hemoglobin derivatives are negative and no bands appear in the spectrum. From the large amounts of globulin and fibrinogen present it is evident that considerable transudation of blood plasma must have occurred; and the normal plasma pigments somewhat concentrated in the thermostat at 37° C. for several days more nearly approach in color the bright yellow of these fluids than do dilute preparations of hemoglobin similarly treated. In our experience, the spinal fluids that definitely contain hemoglobin are somewhat darker, and have rather an amber tint, whereas those giving negative tests for hemoglobin are of a lighter buff yellow color.

Considered from the standpoint of clinical value, all types of yellow spinal fluid are indicative of organic nervous disease, and there are one or two cases on record in which this feature was the determining factor in making that diagnosis. The hemoglobin-containing fluid may conceivably be of value, otherwise, in localizing a cerebral lesion in relation either with the meninges or ventricles. The very general fear of lumbar puncture in cases with signs of brain tumor puts a very definite limitation on the value of spinal fluid examination in general in such cases.

In regard to the Froin compression syndrome we have remarked above that it was of direct importance in enabling us to arrive at the correct diagnosis in our first case. No less an authority than Oppenheim¹¹ has reported 2 cases in which this finding at lumbar puncture clinched the diagnosis of spinal cord tumor, for which without this finding there was insufficient evidence. "After all," he says, "it is no certain indication of a cord-compressing tumor but it makes this opinion very probable. It has given this diagnosis a firm prop in our cases."

Raven,¹⁰ one of Nonne's pupils, who has made especial study of the possible value of spinal fluid examinations in compression of the cord, accepts this syndrome as evidence of compression and very justly states that it tells nothing concerning the nature or the site of the lesion. Notwithstanding these limitations which must be accepted, a glance at the statistics of published cases shows that of 65 cases in which the diagnosis was confirmed by operation, autopsy, or otherwise beyond doubt, about 70 per cent were cases of tumor of the spinal cord or of the vertebræ. Other lesions less frequently found have been enumerated above.

Of 71 cases, in which mention is made of cellular reaction, there was an increased cell count in 38 and a normal count in 33. It is generally held that the cellular increase indicates

some reaction on the part of the meninges, and many authors offer the cellular content of the fluid as a criterion for the differentiation between tumors (without cells) and adhesive inflammatory processes (with cells). We believe that this factor has no very distinct differential value, as witness Case 2 of our report and the fact that of 51 tumors the cells are reported increased in 17, not increased in 23 and not mentioned in 11.

Of 52 cases, in which the location of the lesion was made clear in the reports, 5 were multiple, 8 cervical, 16 thoracic and 23 lumbar.

Nonne's syndrome, the presence of globulin in large amount without cell increase in the cerebrospinal fluid, apparently has much the same significance as the syndrome of Froin. Perhaps, as Hanes²³ suggests, they are merely different stages of the same process, the xanthochromia appearing late; or, as Nonne¹² believes, they may be variants due to the presence or absence of blood. Against Hanes's view might be cited our third case in which the second specimen obtained at a time when the symptoms of compression were much further advanced was water clear and almost normal. Again Demole²⁹ reports a case in which during the single puncture the first flow of yellow fluid quickly changed to a normal one. He interpreted this as indicating such a slight grade of obstruction that the release of pressure below the lesion brought about a change of relationships in the canal and permitted the flow of fluid to be re-established.

Nonne's type of fluid is doubtless of more frequent occurrence with compressive lesions than are xanthochromia and coagulation, but it is not entirely beyond suspicion. Isolated globulin increase is occasionally found in other conditions.

SUMMARY.

We have called attention to the clear, yellow spinal fluids occasionally observed at lumbar puncture. Our remarks are based on 5 cases observed and here reported and an analysis of 100 cases from the literature.

The fluids may be divided into two main groups.

1. Those in which the color is due to dissolved hemoglobin or its derivatives, and which as a rule do not coagulate spontaneously and contain only a small amount of globulin. Such fluids usually are associated with brain tumors in contact with the meninges or ventricles.

2. The larger and more important group comprises those cases showing the so-called Froin's syndrome, in which the fluid is transparently clear, yellow, coagulates spontaneously, contains large amounts of globulin, may or may not show pleocytosis, and gives no positive tests for hemoglobin.

This is a "compression syndrome," its main determinants being the isolation of a lumbar cul-de-sac, in which the spinal fluid stagnates, and probably some vascular changes within its walls.

Clinically, with negative X-ray of the vertebral column, it is strongly suggestive of a tumor of the spinal cord, although it may also be associated with intradural inflammatory processes.

REFERENCES.

1. Froin: Inflammations méningées avec réaction chromatique fibrineuse et cytologique du liquide céphalorachidien. *Gaz. d. hôp., Par.*, 1903, 1005.
2. Froin et Foy: Syndrome de coagulation massive au cours d'une méningite. Action nocive d'une infection sous-arachnoïdienne de collargol. *Gaz. d. hôp., Par.*, 1908, Nov. 18.
3. Aubrey: Le syndrome de coagulation massive du liquide céphalorachidien. Thèse de Paris, 1909.
4. Babinski: Méningite hémorragique fibrineuse. Paraplégie spasmodique lombaire; traitement mercuriel; guérison. *Soc. méd. d. hôp. de Paris*, 1903, Oct. 23, 1083.
5. Cestan et Ravaut: Coagulation en masse et xanthochromie du liquide céphalorachidien dans un cas de pachy-méningo-myélite du cône terminal. *Gaz. d. hôp., Par.*, 1904, Sept. 6.
6. Mestrezat: Le liquide céphalo-rachidien. Paris, 1912, p. 425.
7. Schnitzler: Klinische Beiträge zur Kenntnis der mit Muskelatrophien verlaufenden Formen von multipler Sklerose und chronischer Myelitis. *Ztschr. f. ges. Neurol. u. Psychiat., Berl., u. Leipz.*, 1912, XII, Orig., 310.
8. Siemerling: Gliosis spinalis und Syringomyelie. *Arch. f. Psychiat. u. Nervenkrankh., Berl.*, 1913, L, 449.
9. Klieneberger: Ein eigentümlicher Liquorbefund bei Rückenmarkstumoren. *Monatschr. f. Psychiat. u. Neurol., Berl.*, 1910, XXVIII, 346.
10. Raven: Weitere Beiträge zur Kenntnis des Kompressions-syndroms im Liquor cerebrospinalis. *Deutsche Ztschr. f. Nervenheilk., Leipz.*, 1913, XLIX, 36.
11. Oppenheim (H.): Ueber Caudatumoren unter dem Bilde der Neuralgia schiadica sive lumbosacralis. *Monatschr. f. Psychiat. u. Neurol., Berl.*, 1914, XXXVI, 391.
12. Nonne: Weitere Erfahrungen zum Kapitel der Diagnose von komprimierenden Rückenmarkstumoren. *Deutsche Ztschr. f. Nervenheilk., Leipz.*, 1913, XLVII, 436.
13. Schlesinger: Ueber erfolgreich operierte Rückenmarkstumoren und über das Kompressionssyndrom des Liquor cerebrospinalis. *Wien. klin. Wchnschr.*, 1915, XXVIII, 463.
14. Cooper: Cerebrospinal Fluid of Anomalous Character in a case of Intraspinal Tumor. *Jour. A. M. A.*, 1910, LV, 2298.
15. Greenfield: On the Value of Quantitative Albumin Estimation of the Cerebrospinal Fluid, with special reference to the syndrome of massive coagulation and xanthochromia. *Lancet, Lond.*, 1912, II, 685.
16. Hartman: Multiple Sarcomatosis of the Brain and Spinal Cord. *Texas State J. M., Ft. Worth*, 1914, X, 278.
17. Kennedy and Elsberg: A peculiar undescribed disease of the nerves of the cauda equina. *Am. Journ. Med. Sc., Phila.*, 1914, CXLVII, 645.
18. Collins and Elsberg: Giant tumors of the conus and cauda equina. *Am. Journ. Med. Sc., Phila.*, 1914, CXLVII, 493.
19. Mix: Spontaneous massive coagulation of the cerebrospinal fluid with xanthochromia; its significance in the diagnosis of lesions of the spinal cord and its membranes. *Surg. Clin., Chicago*, 1915, IV, 317.
20. Campbell: Amber color of spinal fluid with coagulation *en masse*. Report of case. *Am. Journ. of Surg.*, 1915, XXIX, 348.
21. Horrax: Studies on the pineal gland. *Arch. Int. Med., Chicago*, 1916, XVII, 627.
22. Bromer: The syndrome of *coagulation massive et xanthochromie* occurring in a case of tuberculosis of the cervical spine. *Am. Journ. Med. Sc.*, 1916, CLI, 378.
23. Hanes: The spinal fluid syndromes of Nonne and Froin and their diagnostic significance. *Am. Journ. Med. Sc.*, 1916, CLII, 66.
24. Raven: Die Bedeutung der isolierten Eiweissvermehrung und der Xanthochromie im Liquor cerebrospinalis für die Diagnose

von Kompression der Rückenmarks. Deutsche Ztschr. f. Nervenheilk., Leipz., 1912, XLIV, 380.

25. Krönig: Histologische und physikalische Lumbalpunktionbefunde und ihre Deutung. Verhandl. d. Congr. f. inn. Med., 17. Congr., 1899, 565.

26. Mohr: Zur Pathologie des Liquor cerebrospinalis. Deutsche Ztschr. f. Nervenheilk., Leipz., 1912, XLIV, 417.

27. Donath: Beitrag zur Landry'schen Paralyse. Wien. klin. Wchnschr., 1905, XVIII, 1327.

28. Reich: Ueber Gelbfärbung der Cerebrospinalflüssigkeit. Mitt., a. d. Grenzgeb. d. Med. u. Chir., Jena, 1913, XXV, 721.

29. Demole: Syndrome de coagulation massive et de xanthochromie dans un cas de compression médullaire par tumeur rachidienne. Rev. Neurol., 1914-1915, XXII, 648.

MULTIPLE SPONTANEOUS INTRACEREBRAL HEMORRHAGES. A CONTRIBUTION TO THE PATHOLOGY OF APOPLEXY.

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Out of 128 cases of intracerebral hemorrhage in 24 (about 18 per cent) the brain showed discrete multiple hemorrhages, none of them being traumatic. The brains were examined because the cause of the coma was in doubt,¹ and trauma had to be excluded. Except two who died on the way to the hospital and four who died in the House of Correction, the patients were all cared for in the Cook County Hospital.

Plurality of hemorrhages, the feature leading to this report, was represented in three brains by three distinct sites of hemorrhage, and in the remaining 21 by two. The combination of one hemorrhage into the internal capsule or basal ganglia and one into the pons was most frequent, occurring in 15 brains (63 per cent). (See diagram of the cerebral circulation, circles A and B.) Of the seven brains (32 per cent) in which both hemorrhages were into the cerebral hemispheres, five presented bilateral symmetrical hemorrhages implicating both internal capsules or basal ganglia. One brain contained hemorrhages into the cerebrum and the cerebellum, and one hemorrhages into the cerebellum and pons. In one brain only did the pontine hemorrhage appear to be primary, a single large clot in the center of the pons being associated with multiple punctate hemorrhages in the left internal capsule.

The appearance of the pontine lesions varied greatly. In eight brains they were numerous and small, scattered irregularly throughout the pontine substance. In seven brains, moderately large hemorrhages occupied the center of the pons, filling the fourth ventricle and surrounding tissue.

The brain receives its blood supply from two sources, the carotids and the vertebrals which anastomose forming a circle or hexagon at the base of the brain beyond which the arteries are practically terminal. The carotids have a more direct route from the aorta than the vertebrals, being straighter and actually shorter. Further, "the diminution in size," according to Tooth,² "is very much more gradual in the vertebral than in the carotid, possibly explaining the lesser liability of

the former to atheroma and rupture. The part of the brain requiring the greatest blood supply is the outside. Therefore, the main divisions of the great vessels are distributed over the cortex by gradual dichotomous division comparable to the usual division of arteries throughout the body. Owing to this, hemorrhage is less common in these than in the internal ones. The vessels of internal distribution come off nearly at right angles from the main trunk. This means greater friction. The vessels are small, have a short course, and are practically terminal. Pressure in them is not much less than in the carotids." For these reasons, hemorrhage is more frequent from the branches of the middle cerebrals supplying the internal capsule and basal ganglia than from the other cerebral arteries.

Following any intracranial hemorrhage there is, as in any case of brain compression, a rise in blood pressure and secondarily a slowing of the pulse, due to stimulation of the vasomotor and vagus centers respectively.³ This means that there is re-established within the arteries a degree of tension in excess of the intracranial tension, which has itself been raised at the time of hemorrhage, owing to the pouring out of blood into a practically closed cavity. The result is an actual increase both in intracranial tension and intra-arterial pressure, which no doubt brings about the rupture of and hemorrhage from other cerebral arteries already weakened by disease. Undoubtedly this is the origin of the hemorrhage from the corresponding branches of the middle cerebral artery of the opposite side occurring in cases of primary internal capsule hemorrhage; the anatomical factors on the two sides are approximately the same; the intra-arterial pressure is actually increased, and the disease of the vessel wall appears as the variable factor. That such changes in blood pressure are not the sole factors determining the production of secondary pontine hemorrhages appears probable in view of the rare occurrence of similar pontine hemorrhages in other conditions of brain compression, as in brain tumor or in extradural hemorrhage, where the mass of extravasated blood may reach

¹ A Consideration of the Relative Frequency of Various Forms of Coma, with Especial Reference to Uremia. Wayne W. Bissell and E. R. LeCount, J. Am. M. Ass., 1915, LXIV, 1041-1045.

² Cerebral Hemorrhage. H. H. Tooth. Allbutt and Rolleston's System of Medicine, VIII, 307: Distribution of Encephalic Hemorrhages. S. W. D. Ludlum. J. Nerv. and Ment. Diseases, 1909, XXXVI, 705.

³ Compression of the Brain. E. von Bergmann in v. Bergmann's System of Medicine. New York, 1904, I, 192: The Blood Pressure Relation of Acute Cerebral Compression, Illustrated by Cases of Intracranial Hemorrhage. H. Cushing. Am. J. Med. Sc., 1903, CXXV, 1017.

a considerable size. Some support for this view was obtained from an examination of the records⁴ and charts of five brain tumors with cerebral arteriosclerosis, and of three cases of spontaneous meningeal hemorrhage with arteriosclerosis; in none was there any pontine hemorrhage.

terminal, resembling in these respects the branches of the middle cerebral artery so frequently the site of primary hemorrhage. The generalized increase in blood pressure following deep intracerebral hemorrhage obviously must occur in the intrapontine arteries as well as elsewhere, and continue even

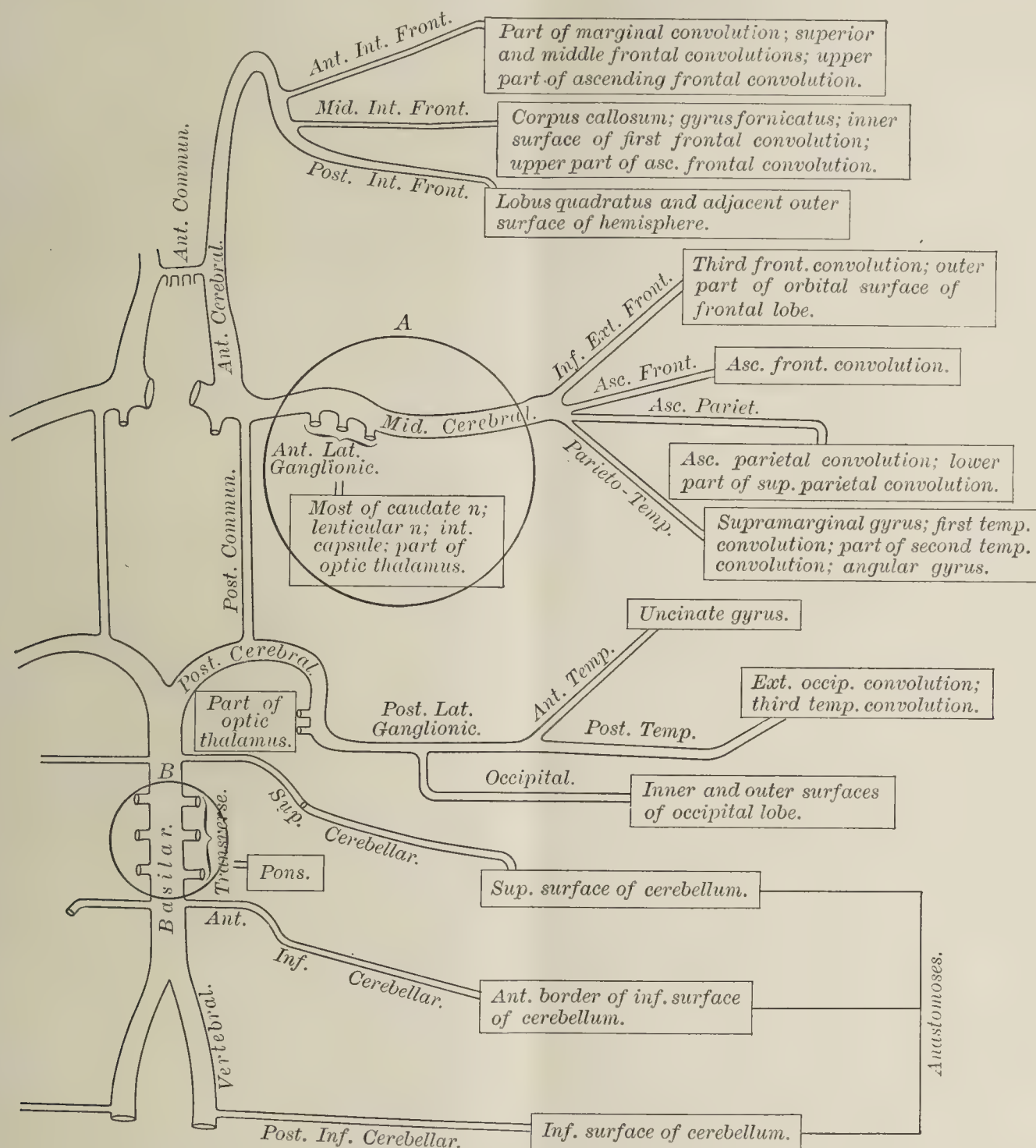


DIAGRAM OF THE BLOOD SUPPLY OF THE BRAIN, A MODIFICATION OF THAT IN FURSAC AND ROSANOFF'S MANUAL OF PSYCHIATRY (BALTIMORE, 1911, P. 339). THE REGIONS A AND B ARE THE MOST FREQUENT SITES OF SPONTANEOUS HEMORRHAGE.

Now, as for this most frequent combination, pontine and deep-seated cerebral hemorrhages, it will be remembered that the pontine arteries are branches of the basilar, just before it divides to form the posterior cerebral arteries, the posterior components of the circle of Willis (see diagram of the cerebral circulation). They are short, small branches, given off nearly at right angles from a large trunk, and are practically

⁴Records of post-mortem examinations in the Pathological Laboratory of Rush Medical College.

after the primary bleeding has been checked by clotting or local pressure or both. When this bleeding has occurred from a branch of the middle cerebral, a lessened amount of blood is sent through this artery and its subdivisions. With the generalized increase in blood pressure referred to, and the absence of any adequate factor of safety to lessen the amount of blood driven with this increased pressure into all the arteries supplying the brain, there is an increased strain in all the other branches of the circle of Willis and perhaps even a back-flow. The site of the greatest strain must be the point of meeting of

the back-flow and the normal flow into the posterior cerebrals from the vertebrals by way of the basilar artery, the exact location depending on the comparative length and peripheral friction of the two channel beds, the carotid and the vertebral. Since this meeting takes place in the posterior part of the system owing to the greater length and more circuitous route of the vertebrals, the pressure throughout the basilar is presumably increased above that in the other arteries, and its branches are subjected to unusual strain. It is probable that the pontine arteries suffer more frequently than the cerebellar, since the latter are safeguarded in some measure by their anastomoses, their greater length and their somewhat greater size. This point might, in future material, be put to a further test by comparing the cases showing ample connecting branches of the circle of Willis and those with narrow or obliterated connectives.

Several reports of multiple spontaneous cerebral hemorrhages have been published.⁵ Most of them are descriptions of single brains containing numerous hemorrhages (2-28), considered chiefly as interesting curiosities.

In the only article which I have so far been able to find, dealing at all comprehensively with multiple spontaneous hemorrhages,⁶ they are described in a general review of 67 cases of pontine hemorrhage, and the issues are confused by failure of the author to differentiate clearly between spontaneous and traumatic hemorrhages. Spontaneous secondary pontine hemorrhages are due, according to Dr. Attwater, "to a general increase in cerebral blood pressure following primary capsular hemorrhages, associated with a degenerate condition of the blood vessels." In support of this explanation he offers a single case of pontine hemorrhage with extradural hemorrhage and skull fracture, ignoring the probable rôle of the obvious trauma in the production of the pontine lesion. Traumatic pontine hemorrhage, on the other hand, is produced, in his opinion, "by a local disturbance of blood pressure in the neighborhood of the pons, due to the movement of the brain and intracranial contents backward and downward toward the foramen magnum, at the moment of impact"; a theory strikingly at variance with the generally accepted view that these hemorrhages are essentially the result of contusions produced by the transmission of a force which is usually sufficient to fracture the base of the skull.⁷ The untenability of any

theory of traumatic hemorrhage by local increase in blood pressure, is apparent in view of the great pressure (4-11 atmospheres, or 16-44 times the normal pressure),⁸ necessary to rupture a normal blood vessel.

Records of 15 cases of traumatic pontine hemorrhages were examined for the purposes of comparison. Twelve of the 15 (80 per cent) occurred with basal skull fracture of the posterior and middle fossæ. In only four (28 per cent) was there a degree of arteriosclerosis sufficient to be detected grossly, in contrast to 67 per cent of the group of secondary spontaneous pontine hemorrhages. The difference in appearance between the two groups is best shown by the diagrams of representative cases (Figs. 1 and 2). The traumatic hemorrhages are almost uniformly punctate, frequently grouped around the periphery of the pons, and connected with small subpial extravasations and numerous lacerations, whereas the spontaneous pontine hemorrhages are remarkably free from such obvious contusions. These differences are frequently of great medico-legal importance.

CONCLUSION.

In the examination of an adequate number of brains containing multiple spontaneous hemorrhages, pontine hemorrhage was found secondary to extensive hemorrhage into the internal capsule and basal ganglia in a majority of cases. The liability of the pontine arteries to secondary rupture is due probably to their anatomic peculiarities (in that they are short, small, terminal branches given off nearly at right angles from a large trunk), and possibly to a disturbance of blood pressure in the circle of Willis with a back-flow into the posterior branches.

EXPLANATION OF PLATE.

FIG. 1.—*Traumatic Intrapontine Hemorrhages*.—A man, aged 50, was brought to the hospital in coma after being struck by an automobile. He died an hour later without regaining consciousness.

Anatomic Findings: Traumatic fracture of skull, 20.9 cm. in length, beginning in the right temple at the line of the suture, going down into the middle of the middle fossa to the right optic foramen, and then passing across to the posterior plate of the ethmoid bone; lacerations and contusions of both temporal lobes; subdural and intraleptomeningeal hemorrhage (wt. 20 gm.) in both middle fossæ; numerous punctate hemorrhages in the pons; traumatic hemorrhages into the pericranial tissues; contusions and lacerations of the face, left forearm and left popliteal space. (This chart and that for Fig. 2 were made by sketching with a paraffin pencil the outlines on glass laid on the brain segments.)

FIG. 2.—*Spontaneous Secondary Intrapontine Hemorrhage*.—A man, aged 60, was on his way to Cook County Hospital for treatment when he suddenly became unconscious on the car. He died within 30 minutes after reaching the hospital, without regaining consciousness.

Anatomic Findings: Spontaneous intracerebral hemorrhage into the right internal capsule and basal ganglia (greatest dimensions 10.5 cm. anteroposteriorly; 6 cm. laterally; 5 cm. from above downward); intrapontine hemorrhage (2.5 cm. x 1.5 cm.—greatest diameters); slight hyperemia of the leptomeninges; marked sclerosis of the basilar artery; fibrous external pachymeningitis.

⁵ 1. Sur un cerveau polyhémorragique. Anglade: J. de méd. de Bordeaux, 1908, XXXVIII, 570. 2. Hémorragie cérébrale récente à foyers multiples. A. Souques, N. iconog. de la Salpêtrière, 1911, XXIV, 193. 3. Double Cerebral Hemorrhage in a Young Man. A. J. Shinnie, Brit. M. J., 1912, II, 780. 4. Hémorragies étendues et multiples des hémisphères cérébraux et du corps calleux. P. Lereboullet, Bull. and Mém. Soc. méd. des hôp. de Paris, 1910, XXX, 534. 5. A Brain with Three Subsequent Hemorrhages. L. Freyburger. Tr. Path. Soc. Lond., 1897, XLIX, 36. 6. Cerveau polyhémorragique. Robert Lafarge, J. de méd. de Bordeaux, 1910, XL, 420.

⁶ Pontine Hemorrhages. H. L. Attwater, Guy's Hosp. Rep., 1911, LXV, 339.

⁷ Ueber Hirnverletzungen durch stumpfe Gewalt und ihre Beziehungen. O. Tillman, Arch. f. Klin. Chir., 1902, LXVI, 750; Etudes expérimentales et cliniques sur les traumatismes cérébraux. H. Duret, Paris, 1878, 39.

⁸ The Blood Flow. Tigerstedt and Murlin. A Text-Book of Human Physiology. New York, 1906, p. 198.

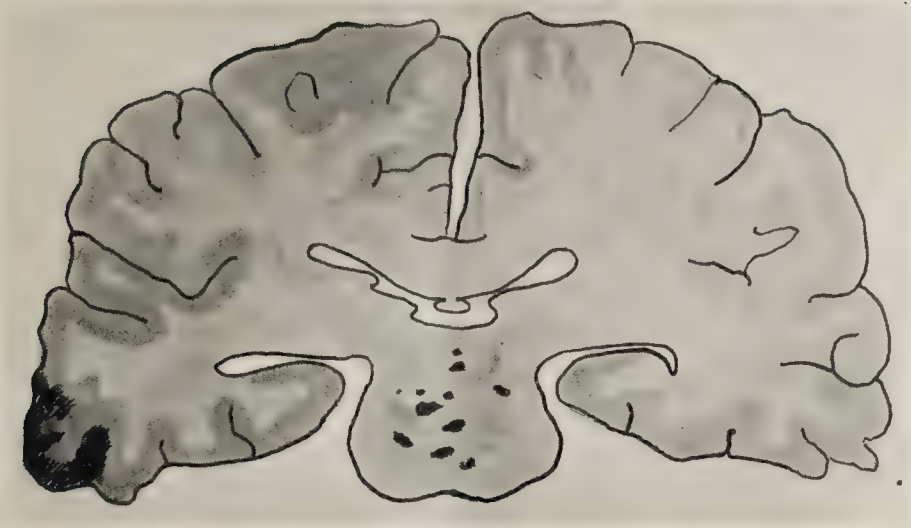


FIG. 1.

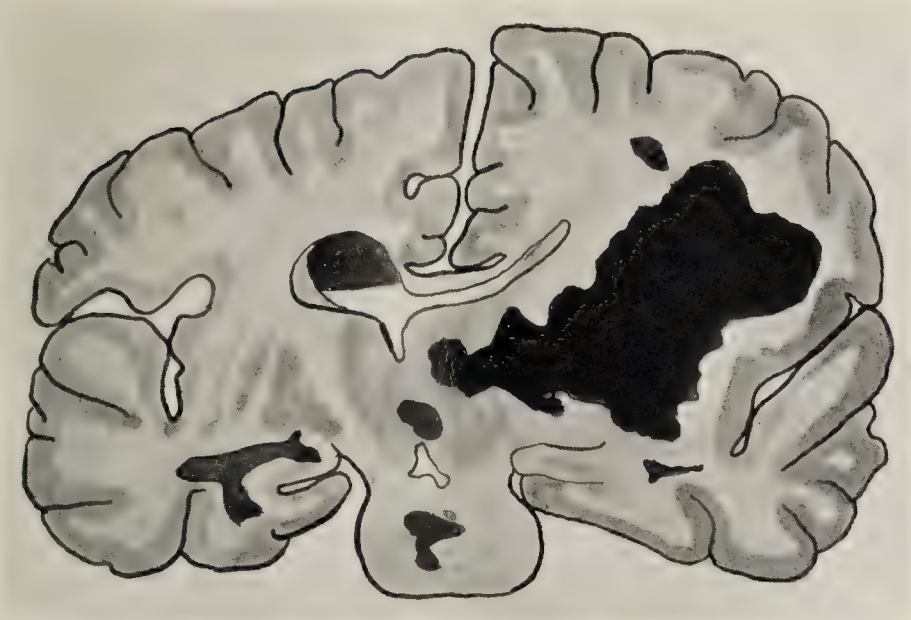


FIG. 2.

TITLES OF PAPERS APPEARING DURING THE YEAR, ELSEWHERE THAN IN THE BULLETIN, BY PRESENT AND FORMER MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF.

- AUER, J.
The action of the depressor nerve on the pupil.—*Am. J. Physiol.*, 1916, xi, 143; also *Proc. Soc. Exper. Biol. & Med.*, 1915-16, xlii, 52.
- AUER, J., and GATES, F. L.
The absorption of adrenalin after intratracheal injection.—*J. Exper. M.*, 1916, xxiii, 757; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 315.
- AUER, J., and MELTZER, S. J.
The intravenous injection of magnesium sulphate for anesthesia in animals.—*J. Exper. M.*, 1916, xxiii, 641; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 287.
The influence of intravenous injections of magnesium sulphate upon the activities of deglutition.—[Abstr.] *Proc. Soc. Exper. Biol. & Med.*, 1916, xlii, 106.
- AUSTRIAN, C. R.
Summer diarrhea and vomiting of childhood.—*Bull. Med. & Chir. Fac. Maryland*, 1916-17, ix, 72.
- AUSTRIAN, C. R., and BLOOMFIELD, A. L.
Observations on the typhoidin reaction.—*Arch. Int. Med.*, 1916, xvii, 663.
- BAETJER, F. H.
Visceroptosis from the radiographer's viewpoint.—*Am. J. Orthop. Surg.*, 1916, xiv, 530.
Pulmonary tuberculosis from a roentgenological standpoint.—*Internat. Clin.*, 1916, 26, s. iii, 124.
The early diagnosis of pulmonary tuberculosis by X-rays. The roentgenological aspect.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 150.
- BAETJER, W. A., BARKER, L. F., and MILLER, S. R.
The clinical diagnosis of acute leukemic states.—*South. M. J.*, 1916, ix, 107.
- BARKER, L. F.
The clinical diagnosis of internal diseases.—N. Y. & Lond., 1916, D. Appleton & Co. 1025; 1063; 1039. p. 8°. Vol. II-IV. Monographic Medicine.
On the growth of medical knowledge concerning the malady known as infantile paralysis, acute anterior poliomyelitis, or the Heine-Medin disease.—*Charlotte (N. C.) M. J.*, 1916, lxxiv, 257.
Relation of the preclinical laboratory courses to the work of the clinical years.—*J. Am. M. Ass.*, 1916, lxvi, 631.
War and the nervous system.—*J. Nerv. & Ment. Dis.*, 1916, xlv, 1.
Development of science of diagnosis.—*J. South. Car. M. Ass.*, 1916, xli, 278.
Syphilis and internal medicine.—*N. York M. J. [etc.]*, 1916, clii, 385.
The teaching of clinical medicine.—*Science*, 1916, n. s., xliii, 799; also *Proc. Ass. Am. M. Coll.*, 1916, 43.
- BARKER, L. F., BAETJER, W. A., and MILLER, S. R.
The clinical diagnosis of acute leukemic states.—*South. M. J.*, 1916, ix, 107.
- BARKER, L. F., and SMITH, F. J.
Functional renal tests (phenolsulphonephthalein; lactose) in orthostatic albuminuria.—*Am. J. M. Sc.*, 1916, cli, 44.
- BAYNE-JONES, S.
Eventration of the diaphragm, with report of a case of right-sided eventration.—*Arch. Int. Med.*, 1916, xvii, 221.
- BEALL, K. H.
Pellagra in Texas.—*South. M. J.*, 1916, ix, 20.
Pellagra.—*Texas State J. M.*, 1916, xii, 170.
- BERKLEY, H. J.
The defective delinquent.—*Maryland Psychiat. Q.*, 1915-16, v.
Mental diseases, etiology.—*Ref. Handb. Med. Sc.*, N. Y., 3d ed., 1916, vi, 392.
- BERNHEIM, B. M.
Saphenopitoneal anastomosis for ascites.—*Am. J. M. Sc.*, 1916, cli, 806.
Choice of operation in the cure of aneurysms of the extremity.—*Interstate M. J.*, 1916, xxiii, 326.
- BERNHEIM, B. M., KING, J. H., and JONES, A. T.
The effect of removal of the spleen upon blood transfusion.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 10.
- BERRY, J. McW.
Orthopedic surgery for nurses.—Phila. & Lond., 1916, W. B. Saunders Co. 97 p. 8°.
Observations on the presence of roentgenological shadows associated with subdeltoid bursitis; also on the presence of similar shadows in other parts of the body.—*Am. J. Orthop. Surg.*, 1916, xiv, 476.
Retarded ossification as an etiologic factor in traumatic arthritis and epiphysitis.—*J. Am. M. Ass.*, 1916, lxvi, 868.
- BLACKFAN, K. D.
Cutaneous reaction from proteins in eczema.—*Am. J. Dis. Child.*, 1916, xi, 441.
- BLOCK, E. B.
The relation of the mammary glands to nervousness and menstruation.—*J. Med. Ass. Georgia*, 1915-16, v, 155.
- BLOCK, E. B., and NYUN, K.
The importance of counting pus cells in the urine.—*South. M. J.*, 1916, ix, 972.
- BLOODGOOD, J. C.
Cancer of the breast; figures which show that education can increase the number of cures.—*J. Am. M. Ass.*, 1916, lxvi, 552.
First aid in accidental wounds.—*Ibid.*, 1916, lxvi, 758.
First aid instruction to police force of Baltimore City.—*Maryland M. J.*, 1916, lix, 34.
American First Aid Conference.—*Ibid.*, 1916, lix, 45.
The objects of the First Aid Conference.—*Mil. Surgeon*, 1916, xxviii, 44; also *Wisconsin M. J.*, 1915-16, xiv, 395.
Control of cancer.—*Pub. Health. Mich.*, 1916, iv, 285.
Primary treatment of accidental wounds.—*South. M. J.*, 1916, ix, 644.
First aid to the injured. A survey of the present experience and prevailing opinion as to the treatment of accidental wounds immediately after the injury.—*Surg., Gynec. & Obst.*, 1916, xxii, 121.
Gas-bacillus infection; surgical bacteriology.—*Ibid.*, 1916, xxiii, 182; also *Tr. Am. Surg. Ass.*, xxxiv, 122.
Cancer investigations.—*Virginia M. Semi-Month.*, 1916, xx, 497.
What every woman should know about cancer of the breast.—*Prevention of Cancer Series*. Pamphlet No. viii, issued by the Council on Health and Public Instruction of Am. M. Ass.
- BLOOMFIELD, A. L., and AUSTRIAN, C. R.
Observations on the typhoidin reaction.—*Arch. Int. Med.*, 1916, xvii, 663.
- BLUMER, G.
The modern medical school: its relations to the hospital and to the medical profession.—*Albany M. Ann.*, 1916, xxxvii, 493.
A note on the simulation of diabetes mellitus.—*Boston M. & S. J.*, 1916, clxxiv, 48.
What attitude should the physician take towards health insurance?—*Penn. M. J.*, 1916, xix, 756.
Importance of anaphylaxis in clinical medicine.—*Providence M. J.*, 1916, xvii, 135.
- BLUMER, G., PEPPER, W., and WOOLLEY, P. G.
The function of the dispensary.—*J. Am. M. Ass.*, 1916, lxvi, 1156; also *Proc. Ass. Am. M. Coll.*, 1916, 99.
- BOGGS, T. R., and PINCOFFS, M. C.
A case of pulmonary monilliasis in the United States.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 62.
- BOGGS, T. R., and WINTERNITZ, M. C.
Acute suppurative hypophysitis as a complication of purulent sphenoidal sinusitis.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 56.
- BREM, W. V.
Blood transfusion, with special reference to group tests.—*J. Am. M. Ass.*, 1916, lxvii, 190.
- BRIDGMAN, E. W., and SCHMEISSER, H. C.
Heart block caused by gumma of the septum.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 90.
- BROWN, HELEN W.
A literary forerunner of Freud.—*Psycho-analyt. Rev.*, 1916, iii.
- BROWN, T. R.
Clinical investigations on intestinal auto-intoxication, especially as regards the question of specificity of toxin.—*Am. J. M. Sc.*, 1916, clii, 845.
A clinical study of the secretions of the digestive tract.—*Boston M. & S. J.*, 1916, clxxv, 775.
Border-line problems in digestive pathology involving both medical and surgical treatment.—*South. M. J.*, 1916, ix, 867.
- BROWN, T. R., and FREEMAN, E. B.
The effect of variations of the gastric secretion upon the composition of the saliva.—*Maryland M. J.*, 1916, lix, 176.
- BUNTING, C. H., and YATES, J. L.
Bacteriological results in chronic leukemia and in pseudoleukemia.—*Stud. Rockefeller Inst. M. Research*, N. Y., 1916, xxiv, 123.
- BURNAM, C. F., and KELLY, H. A.
A résumé of results in the radium treatment of 347 cases of cancer of the uterus and vagina.—*Am. J. Obst.*, 1916, lxxiv, 326.
- BURNS, J. E.
The use of thorium in urology and roentgenology.—*Am. J. Röntgenol.*, 1916, iii, 482.
- BURROW, T.
Permutations within sphere of consciousness.—*J. Abnorm. Psychol.*, 1916-17, xi, 178.
The philology of hysteria: an *a priori* study of the neuroses in the light of Freudian psychology.—*J. Am. M. Ass.*, 1916, lxvi, 783.
- BURROWS, M. T.
The functional relation of intercellular substances in the body to certain structures in the egg cell and unicellular organisms.—[Abstr.] *Anat. Rec.*, 1916, x, 189.
- BYRNES, C. M.
A clinical and pathological study of a condition occurring in the aged usually attributed to cerebral arteriosclerosis.—*J. Nerv. & Ment. Dis.*, 1916, xliii, 489.

CAMERON, D. F.

Variations in renal function dependent on surgical procedures.—*J. Am. M. Ass.*, 1916, lxxvi, 1765.

CAMPBELL, C. M.

The neurotic child; some familiar symptoms and their problems.—*Am. J. Dis. Child.*, 1916, xii, 425.
The relation of social and economic factors to mental hygiene.—*Am. J. Pub. Health*, 1916, vi, 1278.
Constitutional inferiority.—*Maryland Psychiat. Q.*, 1916, vi.
The nature of the dementia in dementia paralytica.—*Psychiat. Bull.*, 1916, ix, 316.

CARTER, D. W., JR.

Hematochyluria; observations on the fat content of the urine and the pathology of the condition.—*Arch. Int. Med.*, 1916, xviii, 541.

CARTER, E. P.

The simple interpretation of polygraphic tracings.—*J. Lab. & Clin. M.*, 1916, i, 719.

CAULK, J. R.

The diagnosis of renal infections—An analytic study of 182 cases.—*Lancet-Clinic*, 1916, cxv, 99.

CAULK, J. R., and GREDITZER, H. G.

Observations on the bladder in diseases of the central nervous system. Report of 50 cases.—*Interstate M. J.*, 1916, xxiii, 36.
Medical and surgical progress. The verumontanum and its diseases. A review of recent literature.—*Ibid.*, 1916, xxiii, 139.
The efficiency of dispensary treatment in chronic infections of the prostate and seminal vesicles.—*Ibid.*, 1916, xxiii, 702.

CHESNEY, A. M.

The latent period in the growth of bacteria.—*J. Exper. M.*, 1916, xxiv, 387.

CHURCHMAN, J. W.

The diagnosis of genito-urinary tuberculosis.—*Med. Rec.*, 1916, lxxxix, 511.

CLARK, A. H.

The interrelation of the surviving heart and pancreas of the dog in sugar metabolism.—*J. Exper. M.*, 1916, xxiv, 621.

CLARK, J. G.

Results obtained by the use of radium in the treatment of cancer of the uterus.—*Ann. Surg.*, 1916, lxxiv, 602.
Phases of the cancer problem.—*J. Med. Soc. N. Jersey*, 1916, xlii, 461.
Final results in 12 cases of colectomy.—*Surg., Gynec. & Obst.*, 1916, xxii, 533.
The treatment of cancer of the uterus.—*Tr. Am. Gynec. Soc.*, 1916, xli, 504.

COLSTON, J. A. C.

Impressions of a year in a French base hospital.—*Johns Hopkins Alumni Mag.*, 1916, iv, 189.
Personal experiences at the Red Cross hospitals at Pau, France.—*Maryland M. J.*, 1916, xlix, 14.

COLSTON, J. A. C., and GORTON, W. S.

The radiographic efficiency of the Coolidge X-ray tube.—*Am. J. Roentgenol.*, 1915-16, n. s., iii, 388.

COOK, H. W.

Peptic ulcer from the point of view of medical selection.—*Med. Rec.*, 1916, lxxxix, 148.
What life insurance companies can do to assist in the control of cancer.—*Ibid.*, 1916, lxxxix, 863.
The obligation of the medical examiner.—*Texas State J. M.*, 1916, xi, 633.

CORNER, G. W.

Mithridatium and theriac. The most famous remedies of old medicine.—*University of California Chronicle*, 1916.

CULLEN, T. S.

Embryology, anatomy, and diseases of the umbilicus, together with diseases of the urachus.—*Phila.*, 1916, W. B. Saunders Co. 701 p. 4°.
The relation of obstetrics, gynecology and abdominal surgery to the public welfare.—*J. Am. M. Ass.*, 1916, lxxvi, 239.
Adenomyoma of the rectovaginal septum.—*Ibid.*, 1916, lxxvii, 401.
Early tuberculosis of the cervix.—*Surg., Gynec. & Obst.*, 1916, xxii, 261.
Adenomyoma of the round ligament and incarcerated omentum in an inguinal hernia, together forming one tumor.—*Ibid.*, 1916, xxii, 258.
The cancer campaign and what it has accomplished.—*Virginia M. Semi-Month.*, 1916, xx, 516.

CUSHING, H.

Headache.—[Abstr.] *Boston M. & S. J.*, 1916, clxxiv, 325.
Hereditary ankylosis of the proximal phalangeal joints (sympalangism).—*Genetics*, 1916, i, 90.
On convulsive spasm of the face produced by cerebellopontine tumors.—*J. Nerv. & Ment. Dis.*, 1916, xlv, 312.
Anosmia and sellar distension as misleading signs in the localization of a cerebral tumor.—*Ibid.*, 1916, xlv, 415.
Concerning operations for the cranio-cerebral wounds of modern warfare.—*Mil. Surgeon*, 1916, xxxviii, 601; xxxix, 22.
Yale in medicine.—In *The Book of the Yale Pageant*, New Haven, 1916. Yale Univ. Press.
With the British medical corps in France.—*Yale Rev.*, 1916, v, 523.

CUSHING, H., and HORRAX, G.

The presence of posterior lobe secretion in the cerebrospinal fluid.—*Proc. Am. Soc. Biol. Chemists*, 1916, p. xxxvii.

CUSHING, H., and WALKER, C. B.

Studies of optic nerve atrophy in association with chiasmal lesions.—*Arch. Ophth.*, 1916, xlv, 407.

DAVIS, D. M., and MARSHALL, E. K., JR.

The influence of the adrenals on the kidney.—*J. Pharmacol. & Exper. Therap.*, 1916, viii, 525; also *Proc. Am. Soc. Biol. Chemists*, 1916, p. xxxvii.

DAVIS, E. G.

Vesical drainage; historical review and presentation of a new apparatus.—*J. Am. M. Ass.*, 1916, lxxvi, 1680.

DAVIS, J. S.

Partial epiphyseal transplantation for defect in fibula. Report of case under observation over five years.—*Ann. Surg.*, 1916, lxxiv, 519.
Plastic and reconstructive surgery.—*J. Am. M. Ass.*, 1916, lxxvii, 338.

DICK, GLADYS R., and DICK, G. F.

Immune reactions in scarlet fever, II. Antigenic properties of bacteria found in scarlatina.—*J. Infect. Dis.*, 1916, xix, 638.

DICK, GLADYS R., DICK, G. F., and RAPPAPORT, B.

A leptothrix associated with chronic hemorrhage nephritis.—*J. Infect. Dis.*, 1916, xviii, 216.

DUFFY, R. N.

The necessity of cystoscopic examinations in the diagnosis of urological lesions; illustrative cases.—*Charlotte (N. C.) M. J.*, 1916, lxxiv, 60.

DUNTON, W. R., JR., and SARGENT, G. F.

Duration of paresis following treatment.—*Am. J. Insan.*, 1916, lxxiii, 241.
Christmas at the Sheppard and Enoch Pratt Hospital.—*Maryland Psychiat. Q.*, 1915-16, v, 70.

ELMENDORF, M. F., and WALKER, J. E.

Hookworm history schedules of two male patients treated with oil of chenopodium at the U. S. Marine Hospital, Wilmington, N. C.—*Virginia M. Semi-Month.*, 1915-16, xx, 552.

EMERSON, C. P.

The mold infections of the lung.—*Indianapolis M. J.*, 1916, xix, 1.
Modern conception of one form of nephritis.—*J. Indiana M. Ass.*, 1916, ix, 105.

EMMONS, A. B.

The profession of medicine; a collection of letters from graduates of the Harvard Medical School.—Cambridge, Mass., 1916, Harvard University Press, 114 p. 8°. Also *Harvard Grad. Mag.*, 1916, xxiv, 477.
Industrial medical supervision.—*Boston M. & S. J.*, 1916, clxxiv, 495.

ERLANGER, J.

Studies in blood pressure estimations by indirect methods. i. The mechanism of the oscillatory criteria.—*Am. J. Physiol.*, 1915-16, xxxix, 401.
Studies in blood pressure estimation by indirect methods. ii. The mechanism of the compression sounds of Korotkoff.—*Ibid.*, 1916, xl, 82.
A note on the contractility of the musculature of the auriculo-ventricular valves.—*Ibid.*, 1916, xl, 150.

ESTES, W. L.

Fractures of the femur.—*Ann. Surg.*, 1916, lxxiv, 74.

EVANS, F. A.

Observations on the origin and status of the so-called "transitional" white blood cell.—*Arch. Int. Med.*, 1916, xvii, 1.
Experimental study of the mononuclear cells of the blood and tissues. With special reference to the so-called transitional cell.—*Ibid.*, 1916, xviii, 692.
The cytology of the exudate in the early stages of experimental pneumonia.—*J. Infect. Dis.*, 1916, xix, 441; also *Proc. Soc. Exper. Biol. & Med.*, 1916, xlii, 99. [Abstr.]
The practical significance of the oxidase reaction as applied to blood cells.—*Proc. N. York Path. Soc.*, 1916, xv, 143.
Gaucher's splenomegaly in a child.—*Ibid.*, n. s. xvi.

EVANS, H. M.

On the behavior of the ovary and especially of the atretic follicle towards vital stains of the azo group.—[Abstr.] *Anat. Rec.*, 1916, x, 264; also *Proc. Soc. Exper. Biol. & Med.*, 1916, xlii, 80.

FELTON, L. D.

Hydrotherapy as applied to psychiatric patients.—*Maryland Psychiat. Q.*, 1915-16, v, 33.

FISHBAUGH, E. C.

Fractional determination of gastric secretions.—*J. Am. M. Ass.*, 1916, lxxvii, 1275.

FISHER, A. L.

Torticollis—a review.—*Am. J. Orthop. Surg.*, 1916, xiv, 669.

FLEXNER, S.

What we know about the transmission of infantile paralysis.—*Am. J. Obst.*, 1916, lxxiv, 338.
A note on the serum treatment of poliomyelitis (infantile paralysis).—*J. Am. M. Ass.*, 1916, lxxvii, 583; also *Science*, 1916, n. s., xlv, 259.
The rapid production of antidyenteric and antimeningococcal sera.—*J. State Med.*, 1916, xxiv, 161; 193.
The nature, manner of conveyance and means of prevention of infantile paralysis.—*J. Am. M. Ass.*, 1916, lxxvii, 279; also *Arch. Pediat.*, 1916, xxxiii, 562; *Med. Times*, 1916, xlv, 239; *Pediatrics*, 1916, xxvii, 341; *Science*, 1916, n. s., xlv, 73; *Wisconsin M. J.*, 1916, xv, 84; *N. York M. J.* [etc.], 1916, civ, 168.

FLEXNER, S., and AMOSS, H. L.

Chemical versus serum treatment of epidemic meningitis.—*J. Exper. M.*, 1916, xxiii, 683; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 239.

FLINT, J. M.

The treatment of fractures by methods of suspension and extension.—*Ann. Surg.*, 1916, lxiii, 641.
 Localization and extraction of projectiles and shell fragments.—*Ann. Surg.*, 1916, lxiv, 151; also *Tr. Am. Surg. Ass.*, 1916, xxxiv, 26.
 The four-post fracture bedstead.—*Ann. Surg.*, 1916, lxiv, 613.
 The organization and problems of a war hospital.—*Mil. Surgeon*, 1916, xxxviii, 405.
 Simple mechanotherapeutic apparatus for military hospitals.—*Surg., Gynec. & Obst.*, 1916, xxiii, 228.

FLOURNOY, H.

Paralysie générale chez une oxycéphalique.—*N. iconog. de la Sal-pétrière*, 1916, xxviii, 15.

FORD, W. W.

Studies on aerobic spore-bearing non-pathogenic bacteria. Part I. Introduction.—*J. Bact.*, 1916, i, 273.
 Studies on spore-bearing non-pathogenic bacteria. Part II. Miscellaneous cultures. Classification.—*Ibid.*, 1916, i, 518; 527.

FORD, W. W., and LAWRENCE, J. S.

Studies on spore-bearing non-pathogenic bacteria. Part I. Spore-bearing bacteria in milk.—*J. Bact.*, i, 277.

FOWLER, H. A.

Remarks on the diagnosis of renal and ureteral calculi.—*Maryland M. J.*, 1916, lix, 183.
 Renorenal reflex pain; report of a case.—*Surg., Gynec. & Obst.*, 1916, xxii, 454.

GARBER, J. R.

Significance of the ammonia co-efficient in obstetrical work.—*South. M. J.*, 1916, ix, 900.

GATCH, W. D.

Instruction of medical students and hospital internes in anesthesia.—*Am. J. Surg.*, 1916, xxx, 98.
 Thoracoplasty for chronic empyema.—*J. Indiana M. Ass.*, 1916, ix, 190.

GERAGHTY, J. T.

Treatment of bladder tumors.—*New York M. J. [etc.]* 1916, clv, 838.

GIFFIN, H. Z.

The treatment by splenectomy of splenomegaly with anemia associated with syphilis.—*Am. J. M. Sc.*, 1916, clii, 5.

GILCHRIST, T. C.

Cancer of the skin.—*Hosp. Bull. Univ. Maryland*, 1915-16, xi, 181.

GILCHRIST, T. C., and KETRON, L. W.

Report of two cases of idiopathic hemorrhagic sarcoma (Kaposi), one presenting unusual features, with special methods of treatment and investigation.—*J. Cutan. Dis. incl. Syph.*, 1916, xxxiv, 429.
 A unique case of atrophy of the fatty layer of the skin, preceded by the ingestion of the fat by large phagocytic cells—macrophages.—*J. Cutan. Dis. incl. Syph.*, 1916, xxxiv, 728.

GILMAN, P. K.

Dermoid tumors of the mouth.—*Surg., Gynec. & Obst.*, 1916, xxii, 672.

GIRDWOOD, J.

The thermometer in the diagnosis of active pulmonary tuberculosis.—*Bull. Med. & Chir. Fac. Maryland*, 1916-17, ix, 74.

GOLDSBOROUGH, F. C.

Toxemias in pregnancy.—*J. Mich. M. Soc.*, 1916, xv, 328.

GOODPASTURE, E. W.

Tumors in relation to senescence in dogs.—*J. Cancer Research*, 1916, i, 363.
 Double primary abdominal pregnancy.—*J. Med. Research*, 1916, xxxiv, 359.

GOODPASTURE, E. W., and CLARK, G.

A study of a toxic substance of the pancreas.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 1.

GOODPASTURE, E. W., and WISLOCKI, G. B.

Old age in relation to cell-overgrowth and cancer.—*J. Med. Research*, 1915-16, xxxiii, 455; also *Johns Hopkins Hosp. Rep.*, 1916, xviii, 4. [Abstr.]

GERRHAM, L. W.

Address to the graduating class of the Glens Falls Hospital Training School for Nurses, October 10, 1916.—*Albany M. Ann.*, 1916, xxxvii, 518.

GORTON, W. S., and COLSTON, J. A. C.

The radiographic efficiency of the Coolidge X-ray tube.—*Am. J. Röntgenol.*, 1915-16, n. s., iii, 388.

GREY, E. G.

Studies on the localization of cerebellar tumors: ii. The pointing reaction and the caloric test.—*Am. J. M. Sc.*, 1916, cli, 693.
 An experimental study of the effect of cholecystgastrostomy on gastric acidity.—*J. Exper. M.*, 1916, xxiii, 15.
 Studies on the localization of cerebellar tumors, the position of the head and suboccipital discomforts.—*Ann. Surg.*, 1916, lxiii, 129.
 On localization of function in the canine cerebellum.—*J. Nerv. & Ment. Dis.*, 1916, xliii, 105.

GRIFFITH, F. W.

The sterile woman.—*South. M. J.*, 1916, ix, 153.

GUNDRUM, F. F., and GRAZER, F.

A study in handicaps.—*Calif. State J. M.*, 1916, xiv, 99.

GWYN, N. B.

Acute yellow atrophy of the liver.—*Ref. Handb. Med. Sc.*, N. Y. 3d ed., 1916, vi, 40.
 Hyperemia of the liver.—*Ibid.*, 1916, vi, 59.

HALSTED, W. S.

An experimental study of circumscribed dilation of an artery immediately distal to a partially occluding band, and its bearing on the dilation of the subclavian artery observed in certain cases of cervical rib.—*J. Exper. M.*, 1916, xxiv, 271.
 As to the cause of the dilatation of the subclavian artery observed in some cases of cervical rib: a clinical and experimental study.—*Tr. Am. Surg. Ass.*, 1916, xxxiv, 273.

HAMMAN, L.

Spontaneous pneumothorax.—*Am. J. M. Sc.*, 1916, cli, 229.

HAMMAN, L., and WOLMAN, S.

Chronic non-tuberculous pulmonary infections.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 171.

HANES, F. M.

The spinal-fluid syndromes of Nonne and Froin and their diagnostic significance.—*Am. J. M. Sc.*, 1916, clii, 66.
 An experimental study of the intraspinal method of therapy in syphilis of the nervous system.—*Old Dominion J. M. & S.*, 1916, xxii, 12.
 Recent advances in the diagnosis and specific treatment of lobar pneumonia.—*Virginia M. Semi-Month.*, 1915-16, xx, 503.

HANES, F. M., and WILLIS, A. M.

Circumscribed cysts of the leptomeninges, with the report of a successful operative case.—*Am. J. M. Sc.*, 1916, clii, 859.

HARRIS, N. MACL.

Milk-sickness.—*Ref. Handb. Med. Sc.*, N. Y., 3d ed., 1916, vi, 522.

HASTINGS, T. W.

Discussion on immunization and its practical applications.—*Tr. Cong. Am. Phys. & Surg.*, 1916, x.

HENDERSON, D. K.

The treatment of drug addiction.—*Glasgow M. J.*, 1916, lxxxv, 190.

HENNINGTON, C. W.

Application of the so-called new war-time antiseptics to the several branches of surgery of civil life.—*Buffalo M. J.*, 1916, lxxii, 163.

HEUER, G. J.

The cerebral nerve disturbances in exophthalmic goitre.—*Am. J. M. Sc.*, 1916, cli, 339.

HIGGINS, W. H.

Medical co-operation in the study of mental efficiency.—*Virginia M. Semi-Month.*, 1916, xxi, 29.

HIRSCHFELDER, A. D.

Studies on the effects of acids.—*J. Am. M. Ass.*, 1916, lxvii, 1891.
 Brain lipid as a hemostatic.—*Science*, 1916, n. s. xlv, 251.

HIRSCHFELDER, A. D., and SCHULTZ, F. W.

Experiences with ethylhydrocuprein in the treatment of measles, scarlet fever and other infections.—*Am. J. Dis. Child.*, 1916, xi, 361.

HITZROT, J. M., and BOLLING, R. W.

Fractures of the neck of the scapula.—*Ann. Surg.*, 1916, lxiii, 215.

HOCH, A.

The problem of syphilitic psychoses.—*J. Nerv. & Ment. Dis.*, 1916, xiv, 170.
 The dementia of the cerebral arteriosclerosis.—*Psychiat. Bull.*, 1916, ix, 306.

HOLMES, J. B.

Recent advances in anatomy, physiology, and pathology of childhood.—*Am. J. Dis. Child.*, 1916, xi, 62.
 Congenital obliteration of the bile ducts: diagnosis and suggestions for treatment.—*Ibid.*, 1916, xi, 405.
 The reliability of the electrical diagnosis of tetany: with especial consideration of the electrical values found in normal children.—*Ibid.*, 1916, xii, 1.
 Multiple abscesses of the brain in infancy.—*Arch. Int. Med.*, 1916, xvii, 591.
 Congenital obliteration of the bile-ducts.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 75.
 Multiple abscesses of the brain in infancy.—*Ibid.*, 1916, xviii, 78.

HOOKER, D. R.

The influence of age upon the venous blood pressure in man.—*Am. J. Physiol.*, 1916, xl, 43.
 Social hygiene—another great social movement.—*Soc. Hyg.*, 1916, ii, 5.

HOPKINS, J. G., and ZINSSER, H.

On a species of *Treponema* found in rabbits.—*J. Bact.*, 1916, i, 489.
 Studies on *Treponema pallidum* and syphilis. ii. Spirochaeticidal antibodies against *Treponema pallidum*.—*J. Exper. M.*, 1916, xxiii, 323.
 Studies on *Treponema pallidum* and syphilis. iii. The individual fluctuations in virulence and comparative virulence of *Treponema pallidum* strains passed through rabbits.—*Ibid.*, 1916, xxiii, 329.

HOPKINS, J. G., ZINSSER, H., and MCBURNEY, M.

Studies on *Treponema pallidum* and syphilis. iv. The difference in behavior in immune serum between cultivated non-virulent *Treponema pallidum* and virulent treponemata from lesions.—*J. Exper. M.*, 1916, xxiii, 341.
 Studies on *Treponema pallidum* and syphilis. v. Further studies on the relation of culture pallida to virulent pallida and on reinfection phenomena.—*Ibid.*, 1916, xxiv, 561.

HOWARD, C. P.

The symptoms and physical signs resulting from wounds of the chest.—*Am. J. M. Sc.*, 1916, clii, 650.

HOWELL, W. H.

Structure of the fibrin-gel and theories of gel-formation.—*Am. J. Physiol.*, 1916, xl, 526.

HOWLAND, J.

Acidosis in infancy and childhood.—*Tr. Ass. Am. Phys.*, 1916, xxxi.

HOWLAND, J., and HOLT, L. E.

Diseases of infancy and childhood.—7 ed. N. Y. & Lond., 1916, D. Appleton & Co., 1161 p. 8°.

HOWLAND, J., HAESLER, F. H., and MARRIOTT, W. MCK.

The use of a new reagent for microcolorimetric analysis as applied to the determination of calcium and of inorganic phosphates in the blood serum.—*Proc. Am. Soc. Biol. Chemists*, 1916, p. xviii.

HOWLAND, J., and MARRIOTT, W. MCK.

Acidosis occurring with diarrhea.—*Am. J. Dis. Child.*, 1916, xl, 309. Acetone body production in infancy and childhood.—*Ibid.*, 1916, xii, 459.

Phosphate retention as a factor in the production of acidosis in nephritis.—*Arch. Int. Med.*, 1916, xviii, 708.; also *Tr. Am. Soc. Adv. Clin. Investigation*, 1916, viii.

A discussion of acidosis, with special reference to that occurring in the diseases of childhood.—*Arch. Pediat.*, 1916, xxxiii, 124; also *Am. J. Obst.*, 1916, lxxiii, 556; *Med. Rec.*, 1916, lxxxix, 125.

The calcium content of the blood in rickets and tetany.—*Tr. Am. Pediat. Soc.*, 1916, xxviii.

HUNNER, G. L.

Stricture of the ureter. Excluding tuberculosis and calculus; report of 50 cases.—*N. York M. J. [etc.]*, 1916, civ, 5.

Treatment of ureteral stricture with special reference to retrograde dilatation.—*South. M. J.*, 1916, ix, 616.

HURD, H. M.

Some sources of friction in the management of hospitals.—*Mod. Hosp.*, 1916, vi, 30.

Another source of friction in hospital administration.—*Ibid.*, 1916, vi, 112.

Who shall manage the training school for nurses?—*Ibid.*, 1916, vi, 114. Advantages of the budget system.—*Ibid.*, 1916, vi, 186.

Nathan Smith, Nathan R. Smith, and Alan P. Smith—a medical family.—*Maryland M. J.*, 1916, lix, 56; also *Bull. Med. & Chir. Fac. Maryland*, 1915-16, viii, 157.

Need of segregation of imbecile women.—*Maryland Psychiat. Q.*, 1915-16, v, 64.

HURD, H. M. [and others].

The institutional care of the insane in the United States and Canada. 2 v. Balt., 1916, Johns Hopkins Press. 497; 897 p. 8°.

HURWITZ, S. H.

Preliminary tests of the blood in transfusions.—*Calif. State J. M.*, 1916, xiv, 318.

HURWITZ, S. H., and LUCAS, W. P.

A study of the blood in hemophilia.—*Arch. Int. Med.*, 1916, xvii, 543.

HURWITZ, S. H., and MEYER, K. F.

Studies on the blood proteins. 1. The serum globulins in bacterial infection and immunity.—*J. Exper. M.*, 1916, xxiv, 515.

HURWITZ, S. H., and TRANTER, C. L.

On the reaction of the cerebrospinal fluid.—*Arch. Int. Med.*, 1916, xvii, 828.

HUTCHINS, H. T.

The rôle of the anteposed uterus in the causation of backache and pelvic symptoms.—*J. Am. M. Ass.*, 1916, lxvii, 940.

INGRAHAM, C. B.

The etiology and diagnosis of endometritis.—*Colorado Med.*, 1916, xiii, 19.

JANEWAY, T. C.

Management of patients with chronic renal disease.—*Am. J. M. Sc.*, 1916, cli, 157; also *Bull. Med. & Chir. Fac. Maryland*, 1915-16, viii, 103.

The etiology of the diseases of the circulatory system. (Shattuck lecture.)—*Boston M. & S. J.*, 1916, clxxiv, 915.

JELKS, E., and PEYTON, H. A.

Pyelography as an aid to the diagnosis of certain obscure renal and abdominal conditions.—*J. Florida M. Ass.*, 1916, iii, 129.

JONES, W.

Presidential address. An indirect method of determining pyrimidine groups in nucleotides.—[Abstr.] *Proc. Am. Soc. Biol. Chemists*, 1916, p. x.

The admissibility of ammonium magnesium phosphate as a form in which to weigh phosphoric acid.—*J. Biol. Chem.*, 1916, xxv, 87.

JONES, W., and GERMANN, H. C.

Hydrolysis of yeast nucleic acid with ammonia.—*J. Biol. Chem.*, 1916, xxv, 93.

KEITH, N. M., and LAMSON, P. D.

The rôle of the liver in acute polycythemia. iii. The relation of plasma volume to the number of erythrocytes per unit volume of blood.—*J. Pharmacol. & Exper. Therap.*, 1916, viii, 247.

KELLY, H. A.

Some radium achievements.—*Am. J. Surg.*, 1916, xxx, 73.

Double shame of Baltimore. Her unpublished vice report, her indifference.—*Delaware State M. J.*, 1916, vii, 2.

Radium therapy in cancer of the uterus.—*Tr. Am. Gynec. Soc.*, 1916, xli, 532.

Radiotherapy.—*Tr. M. Ass. Alabama*, 1916.

Radium and lymphosarcoma.—*Tr. South. Surg. & Gynec. Ass.*, 1916, xxix.

Treatment of fibroid tumors with radium.—*Woman's M. J.*, 1916, xxvi.

KELLY, H. A., and BURNAM, C. F.

A résumé of results in the radium treatment of 347 cases of cancer of the uterus and vagina.—*Am. J. Obst.*, 1916, lxxiv, 326.

Radium in the treatment of carcinomas of the cervix uteri and vagina.—*Radium*, 1916, vi, 73; also *Tr. Am. Gynec. Soc.*, 1916, xli.

Treatment of lymphosarcoma with radium.—*Tr. South. Surg. & Gynec. Ass.*, 1916, xxix.

KELLY, H. A., and NEILL, W.

Cauterization and fulguration of bladder tumors.—*J. Am. M. Ass.*, 1916, lxvi, 721.

KEMPF, E. J.

Two methods of subjective learning in the monkey, *Macacus rhesus*.—*J. Animal Behavior*, 1916, vi, 256.

Did consciousness of self play a part in the behavior of this monkey?—*J. Philos. Psychol. [etc.]*, 1916, xlii, 410.

KETRON, L. W., and GILCHRIST, T. C.

Report of two cases of idiopathic hemorrhagic sarcoma (Kaposi), one presenting unusual features, with special methods of treatment and investigation.—*J. Cutan. Dis. incl. Syph.*, 1916, xxxiv, 429.

A unique case of atrophy of the fatty layer of the skin, preceded by the ingestion of the fat by large phagocytic cells—macrophages.—*Ibid.*, 1916, xxxiv, 728.

KETRON, L. W., and KING, J. H.

Gastro-intestinal findings in acne vulgaris, especially fluoroscopic.—*J. Am. M. Ass.*, 1916, lxvii, 671.

KING, J. H.

The effect of removal of the spleen upon the metabolism in dogs. Preliminary report.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 7.

KING, J. H., BERNHEIM, B. M., and JONES, A. T.

The effect of removal of the spleen upon blood transfusion.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 10.

KING, J. H., and KETRON, L. W.

Gastro-intestinal findings in acne vulgaris, especially fluoroscopic.—*J. Am. M. Ass.*, 1916, lxvii, 671.

KING, J. T., JR.

The quantitative effect of salvarsan on the Wassermann reaction of the blood.—*J. Am. M. Ass.*, 1916, lxvii, 1669.

KNOX, J. H. M.

A case of acute myelogenous leukemia in an infant.—*Am. J. Dis. Child.*, 1916, xl, 462.

The diet of children after infancy.—*J. Am. M. Ass.*, 1916, lxvii, 432.

Infant welfare work; its necessity—its reward.—*Maryland M. J.*, 1916, lix, 170; also *Pediatrics*, 1916, xxviii, 490.

Report of a case of myelogenous leukemia in an infant nine months old.—*Pediatrics*, 1916, xxviii, 74.

KNOX, J. H. M., WAHL, H. R., and SCHMEISSER, H. C.

Gaucher's disease. A report of two cases in infancy.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 64.

KRAUSE, A. K.

Attempts to alter the resistance of guinea pigs to tuberculous infection and extension by anaphylactic shock.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 231.

Experimental studies on cutaneous hypersensitiveness to tuberculo-protein.—*Ibid.*, 1916, xii, 233.

Some unusual consequences of artificial pneumothorax.—*Ibid.*, 1916, xii, 234.

Cellular or tissue immunity to tuberculosis and its relation to the pathology of tuberculosis.—*Ibid.*, 1916, xii, 243.

Studies in immunity to tuberculosis. Experimental studies on the cutaneous reaction to tuberculo-protein. First paper. Factors governing the reaction.—*J. Med. Research*, 1916, xxxv, 1.

Studies in immunity to tuberculosis. The anaphylactic state in its relation to resistance to tuberculous infection and tuberculous disease. An experimental study.—*Ibid.*, 1916, xxxv, 25.

Studies in immunity to tuberculosis. Concerning the general tuberculin reaction.—*Ibid.*, 1916, xxxv, 43.

How we can help the tuberculous.—*J. Outdoor Life*, 1916, xlii, 372.

Edward L. Trudeau: a study.—*Med. Pickwick*, 1916, ii, 83.

LANDOIS, F., and BURCKHARDT, H.

Erfahrungen über die Behandlung inficierter Gelenke im Kriege.—*Beitr. z. klin. Chir.*, 1916, xcvi, 358.

LAWLER, ELSIE M.

How much time should be allowed for specialization during the training school course?—*Johns Hopkins Nurses Alumnae Mag.*, 1916, iv, 248; also *Am. J. Nursing*, 1916, xvi, 839.

LEONARD, V. N., and DAYTON, A. B.

Multiple acute gastric ulcers after using Percy's "Cold iron" for inoperable carcinoma; preliminary report of a fatal case.—*J. Am. M. Ass.*, 1916, lxvi, 1549.

LEVY, R. L.

Conditions of activity in endocrine glands. Effect of thyroid secretion on pressor action of epinephrin.—*Am. J. Physiol.*, 1916, xli, 492.

- LEVY, R. L., and ROWNTREE, L. G.
On the toxicity of various commercial preparations of emetin hydrochlorid.—*Arch. Int. Med.*, 1916, xvii, 420.
A study of the buffer value of the blood.—*Ibid.*, 1916, xvii, 525.
- LEWIS, D. S., and MOSENTHAL, H. O.
A comparative study of tests for renal function: Phenolsulphonephthalein, nonprotein nitrogen and urea nitrogen of the blood, Ambard's coefficient of urea excretion and the test meal for renal function.—*J. Am. M. Ass.*, 1916, lxvii, 933.
- LISSE, H.
The eye, ear, nose and throat in disease of the thyroid and thymus.—*Ophth. Rec.*, 1916, xxv, 433.
- LYMAN, D. R.
The development of the tuberculosis crusade and its needs.—*Lancet-Clinic*, 1916, cxvi, 193.
A case of unsuspected spontaneous pneumothorax.—*Tr. Am. Climat. Ass.*, 1916, xxxii.
- MACCALLUM, W. G.
A text-book of pathology. Phila., 1916, W. B. Saunders Co. 1100 p. 8°.
- McCLURE, R. D.
Pernicious anemia treated by splenectomy and systematic, often-repeated transfusion of blood; transfusion in benzol poisoning.—*J. Am. M. Ass.*, 1916, lxvii, 793.
- McCLURE, W. B., HOFFMAN, W. H., and SAUER, L. W.
Simultaneous injections of streptococci and dahlia in the guinea-pig.—*J. Infect. Dis.*, 1916, xviii, 353.
- McCRAE, T.
An epidemic of pneumococcus infection.—*Canad. M. Ass. J.*, 1916, vi, 769.
Chronic arthritis.—*Penn. M. J.*, 1916, xix, 501.
The separation of tuberculosis from general medicine.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 83.
- McCRAE, T., and COPLIN, W. M. L.
Gelatinoid carcinoma (morbus gelatinosus) of the peritoneum.—*Am. J. M. Sc.*, 1916, cli, 475.
- McCRAE, T., and FUNK, E. H.
Bronchiectasis of the upper lobes, with report of five cases with necropsies.—*J. Am. M. Ass.*, 1916, lxvii, 1060.
- MACKENZIE, J. N.
Some reminiscences, reflections and confessions of a laryngologist.—*J. Laryngol.*, 1916, xxxi, 411; also *Ann. Otol., Rhinol. & Laryngol.*, 1916, xxv, 61.
- MAJOR, R. H.
The work at Rosedale. [University of Kansas School of Medicine.]—*Kansas M. J.*, 1916, xvi, 106.
- MALL, F. P.
On the study of racial embryology.—Johns Hopkins Univ., Dept. Embryology, 1916. Pamphlet. (Privately printed.)
The human magna reticulæ in normal and in pathological development.—*Wash.*, 1916, Carnegie Inst., Wash., Publ. No. 224.
On several anatomical characters of the human brain said to vary according to race and sex, with especial reference to the weight of the frontal lobe.—*Atlanta Univ. Publ.*, 1916, No. 20.
- MARRIOTT, W. McK.
Progress in pediatrics: review of the literature on the metabolism of normal infants.—*Am. J. Dis. Child.*, 1916, xii, 88.
A method for the determination of the alkali reserve of the blood plasma.—*Arch. Int. Med.*, 1916, xvii, 840.
The therapeutic value of the hypophosphites.—*J. Am. M. Ass.*, 1916, lxvi, 486.
The determination of alveolar carbon dioxide tension by a simple method.—*Ibid.*, 1916, lxvi, 1594.
A simplified procedure for the determination of the carbon dioxide tension in the alveolar air.—*Proc. Am. Soc. Biol. Chemists*, 1916, p. xviii.
- MARRIOTT, W. McK., and HOWLAND, J.
Acidosis occurring with diarrhea.—*Am. J. Dis. Child.*, 1916, xi, 309.
Acetone body production in infancy and childhood.—*Ibid.*, 1916, xii, 459.
Phosphate retention as a factor in the production of acidosis in nephritis.—*Arch. Int. Med.*, 1916, xviii, 708; also *Tr. Am. Soc. Adv. Clin. Investigation*, 1916, viii.
A discussion of acidosis, with special reference to that occurring in the diseases of childhood.—*Arch. Pediat.*, 1916, xxxiii, 124; also *Am. J. Obst.*, 1916, lxxiii, 556; *Med. Rec.*, 1916, lxxxix, 125.
The calcium content of the blood in rickets and tetany.—*Tr. Am. Pediat. Soc.*, 1916, xxviii.
- MARRIOTT, W. McK., HOWLAND, J., and HAESLER, F. H.
The use of a new reagent for microcolorimetric analysis as applied to the determination of calcium and of inorganic phosphates in the blood serum.—*Proc. Am. Soc. Biol. Chemists*, 1916, p. xviii.
- MARSHALL, H. T.
Osteoma.—*Ref. Handb. Med. Sc.*, N. Y. 3d ed. 1916, vi, 925.
- MARSHALL, H. W.
A case of multiple cartilaginous exostoses.—*Am. J. Orthop. Surg.*, 1916, xiv, 346.
Chronic backache.—*Boston M. & S. J.*, 1916, clxxiv, 591.
- MEYER, A.
The scope of psychopathology.—*Psychiat. Bull.*, 1916, ix, 297.
The extra-institutional responsibilities of state hospitals for mental diseases.—*Proc. Joint Board Trustees, State Hosp. Mich.*, 1916, 5.
Mental diseases, pathology.—*Ref. Handb. Med. Sc.*, N. Y., 3d ed., 1916, vi, 400.
The right to marry. What can a democratic civilization do about heredity and child welfare?—*Survey*, 1916, xxxvi, 243.
- MILLER, G. B.
Etiology of sterility in women.—*Am. J. Obst.*, 1916, lxxiv, 450.
- MILLER, R. T.
Acute suppurative pancreatitis. Gangrene of the major portion of the pancreas. Recovery. Determination of pancreatic function three years subsequently.—*Ann. Surg.*, 1916, lxiv, 320.
Retroperitoneal rupture of the duodenum by blunt force.—*Ann. Surg.*, 1916, clxi, 48.
The surgical treatment of ascites. Direct drainage of the fluid into the blood stream by implantation of the saphenous vein in the peritoneum; report of five cases.—*Penn. M. J.*, 1915-16, xix, 413.
- MILLER, S. R., BAETJER, W. A., and BARKER, L. F.
The clinical diagnosis of acute leukemic states.—*South. M. J.*, 1916, ix, 107.
- MINOT, G. R.
Studies on a case of idiopathic purpura hemorrhagica.—*Am. J. M. Sc.*, 1916, clxi, 48.
Methods for testing donors for transfusion of blood and consideration of factors influencing agglutination and hemolysis.—*Boston M. & S. J.*, 1916, clxxiv, 667.
The effect of temperature upon the clotting time (prothrombin time) of oxalated plasma with calcium.—*J. Med. Research*, 1915-16, xxxiii, 503.
- MINOT, G. R., and DENNY, G. P.
The coagulation of blood in the pleural cavity.—*Am. J. Physiol.*, 1915-16, xxxix, 455.
- MINOT, G. R., DENNY, G. P., and DAVIS, D.
Prothrombin and antithrombin factors in the coagulation of blood.—*Arch. Int. Med.*, 1916, xvii, 101.
- MINOT, G. R., and LEE, R. I.
The blood platelets in hemophilia.—*Arch. Int. Med.*, 1916, xviii, 474.
- MINOT, G. R., LEE, R. I., and VINCENT, B.
Splenectomy in pernicious anemia; studies on bone marrow stimulation.—*J. Am. M. Ass.*, 1916, lxvii, 719.
- MINOT, G. R., and SELLARDS, A. W.
The antagonistic action of negative sera upon the Wassermann reaction.—*J. Med. Research*, 1916, xxxiv, 131.
Injection of hemoglobin in man and its relation to blood destruction, with especial reference to the anemias.—*Ibid.*, 1916, xxxiv, 469.
- MORRIS, R. S.
The glucose content of the blood.—(Editorial.) *J. Lab. & Clin. M.*, 1916, i, 208.
Laboratory methods. Methods for the determination of glucose in the blood.—*Ibid.*, 1916, i, 252.
The uric acid of the blood.—*Ibid.*, 1916, i, 454.
The presence of eosinophile cells in pleural exudates.—*Ibid.*, 1916, i, 540.
Recent studies on hemophilia.—*Ibid.*, 1916, i, 714.
Tonsillectomy during the course of acute rheumatic fever.—*Ibid.*, 1916, ii, 168.
- MORRIS, R. S., and WOOLLEY, P. G.
The clinic and autopsy room.—*Lancet-Clinic*, 1916, cxvi, 66, 89, 164, 233, 258, 398, 401, 404, 475, 522.
- MORRIS, W. H.
Secondary hemorrhage in military surgery.—*Mil. Surgeon*, 1916, xxxviii, 131.
- MOSENTHAL, H. O.
The treatment of diabetes mellitus.—*J. Med. Soc. N. Jersey*, 1916, xiii, 339.
- MOSENTHAL, H. O., and LEWIS, D. S.
A comparative study of tests for renal function; phenolsulphonephthalein, nonprotein nitrogen and urea nitrogen of the blood, Ambard's coefficient of urea excretion, and the test meal for renal function.—*J. Am. M. Ass.*, 1916, lxvii, 933.
- MOSENTHAL, H. O., and RICHARDS, A. E.
The interpretation of a positive nitrogen balance in nephritis.—*Arch. Int. Med.*, 1916, xvii, 329.
- NAFFZIGER, H. C.
Prospects of surgical treatment in meningitis.—*Calif. State J. M.*, 1916, xiv, 322.
Certain eye and ear affections in association with head injuries.—*Ophth. Rec.*, 1916, xxv, 502.
- NEEL, J. C.
Retroadplacements of the uterus; with especial reference to their causation and a new method of treatment.—*Calif. State J. M.*, 1916, xiv, 372.
Retroadplacements of the uterus.—*Surg. Gynec. & Obst.*, 1916, xxii, 233.
- NIXON, P. I.
Chaparro amargosa in the treatment of amebic dysentery.—*J. Am. M. Ass.*, 1916, lxvi, 946.
The intravenous use of mercuric chlorid. A note on a new method of administration; with special reference to prevention of vein obliteration.—*J. Am. M. Ass.*, 1916, lxvi, 1622.
Can we diagnose appendicitis?—*Med. Rec.*, 1916, lxxxix, 469.

NUTTING, M. A.

A sounder economic basis for training schools for nurses.—*Am. J. Nursing*, 1916, xvi, 310.
Education of nurses for the home and the community.—*Mod. Hosp.*, 1916, vi, 196.

OSLER, SIR W.

Science and war; an address delivered at University of Leeds Medical School.—*N. Y.*, 1916, Oxford Univ. 39 p. 8°.
The tuberculous soldier.—*Lancet*, 1916, ii, 220.
Local tetanus.—(Correspondence.) *Ibid.*, 1916, ii, 877.
[Remarks.] General news.—*Mil. Surgeon*, 1916, xxxix, 232.
Treatment of cerebro-spinal meningitis.—*Practitioner*, 1916, xcvi, 1.
Discussion on paratyphoid fever.—*Proc. Roy. Soc. Med.*, Lond., 1915-16, ix, Med. Sect., 38.
Discussion on trench nephritis.—*Ibid.*, Lond., 1915-16, ix, Med. Sect., xiv.

OSLER, SIR W., ROBB, A. G. [et al.]

Discussion on the treatment of cerebrospinal meningitis.—*Proc. Roy. Soc. Med.*, Lond., 1915-16, ix, Therap. & Pharmacol. Sect., 1.

PARFITT, C. D.

The adjustment of pressure in induced pneumothorax. With special regard to the mobility of the mediastinum as indicated by the manometer.—*Arch. Int. Med.*, 1916, xvii, 646.
Tuberculosis often of secondary importance to other pathological conditions.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 118.

PARK, E. A.

Review of the literature of the past two years on the organs of internal secretion.—*Am. J. Dis. Child.*, 1916, xii, 477.

PEABODY, F. W.

Some aspects of the clinical study of the respiration: the significance of alveolar air analysis.—*Am. J. M. Sc.*, 1916, cli, 184.
Tests of renal function from the standpoint of the general practitioner.—*Boston M. & S. J.*, 1916, clxxv, 158.
Some factors in the production of cardiac dyspnea.—*J. Am. M. Ass.*, 1916, lxvii, 1136.

PEABODY, F. W., HIGGINS, H. L., and FITZ, R.

Study of acidosis in three normal subjects, with incidental observations on the action of alcohol as an antiketogenic agent.—*J. Med. Research*, 1916, xxxiv, 263.

PEABODY, F. W., MEYER, A. L., and DUBOIS, E. F.

Clinical calorimetry. xvi. The basal metabolism of patients with cardiac and renal disease.—*Arch. Int. Med.*, 1916, xvii, 980.

PEARCE, LOUISE.

Klossiella infection of the guinea-pig.—*J. Exper. M.*, 1916, xxiii, 431; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 189.

PEARCE, LOUISE, and BROWN, W. H.

(Chemopathological studies with compounds of arsenic. i. Types of the arsenic kidney.—*Stud. Rockefeller Inst. M. Research*, N. Y., 1916, xxiv, 75.
(Chemopathological studies with compounds of arsenic. ii. Histological changes in arsenic kidneys.—*Ibid.*, 1916, xxiv, 83.
(Chemopathological studies with compounds of arsenic. iii. On the pathological action of arsenicals on the adrenals.—*Ibid.*, 1916, xxiv, 93.
(Chemopathological studies with compounds of arsenic. iv. The character and distribution of renal injury produced by arsenicals as indicated by the processes of repair.—*J. Exper. M.*, 1916, xxiii, 443; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 189.

PENROSE, C. A.

The three phases of life.—*Maryland M. J.*, 1916, lix, 37.

PLAGGEMEYER, H. W.

Tuberculosis of the seminal duct.—*J. Mich. M. Soc.*, 1916, xv, 118.
Tuberculosis of the seminal vesicle and epididymis.—*Urol. & Cutan. Rev.*, 1916, xx, 134.

PLASS, E. D.

A fatal case of multiple primary carcinomata.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 66.
Fetal and placental syphilis.—*Am. J. Obst.*, 1916, lxxiv, 561; also *Tr. Am. Gynec. Soc.*, 1916, xli, 348.

RANDALL, A.

The relation of bladder tumors to the cancer problem.—*Therap. Gaz.* [etc.], 1916, 3. s. xxxii, 242.

RANDOLPH, R. L.

A case of blepharochalasis, a variety of dermatolysis.—*Ophth. Rec.*, 1916, xxv, 616; also *Tr. Am. Ophth. Soc.*, 1916, xiv, 518.
A case of congenital suppurative choroiditis with microphthalmos.—*Ophth. Rec.*, 1916, xxv, 619.

RANDOLPH, R. L., and SCHMEISSER, H. C.

A clinical and pathological study of two cases of miliary tubercles of the choroid.—*Tr. Am. Ophth. Soc.*, 1916, xiv, 585.

REID, M. R.

Partial occlusion of the aorta with the metallic band. Observations on blood pressures and changes in the arterial walls.—*J. Exper. M.*, 1916, xxiv, 287; also *Tr. Am. Surg. Ass.*, 1916, xxxiv, 289.

REMSEN, C. M.

Suggested operative steps dealing with spontaneous intracerebral hemorrhage (apoplexy).—*Ann. Surg.*, 1916, lxiii, 513.
The relation of the pathological basis of hydrocephalus to its surgical alleviation.—*Interstate M. J.*, 1916, xxiii, 89.
The acute typhoid abdomen; with especial reference to surgical complications.—*J. Am. M. Ass.*, 1916, lxvi, 28.

REMSEN, C. M., and CRENSHAW, H.

A case of hemiparesis, ataxia and astereognosis associated with arachnoidal edema.—*J. Am. M. Ass.*, 1916, lxvi, 262.

RIGGS, T. F.

End-to-end suture of the bile-ducts.—*Surg., Gynec. & Obst.*, 1916, xxii, 660.

ROUS, P.

The influence of dieting upon the course of cancer.—*Stud. Rockefeller Inst. M. Research*, N. Y., 1916, xxiii, 7.

ROUS, P., and JONES, F. S.

A method for obtaining suspensions of living cells from the fixed tissues, and for the plating out of individual cells.—*J. Exper. M.*, 1916, xxiii, 549; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 219.
The protection of pathogenic micro-organisms by living tissue cells.—*Ibid.*, 1916, xxiii, 601; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 227.

ROUS, P., and TURNER, J. R.

The preservation of living red blood cells *in vitro*. i. Methods of preservation.—*J. Exper. M.*, 1916, xxiii, 219; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 107.
The preservation of living red blood cells *in vitro*. ii. The transfusion of kept cells.—*Ibid.*, 1916, xxiii, 239; also *Stud. Rockefeller Inst. M. Research*, 1916, xxv, 127.

ROWNTREE, L. G.

Investigations in diagnosis and treatment of acidosis.—*Tr. Ass. Am. Phys.*, 1916, xxxi.

ROWNTREE, L. G., and LEVY, R. L.

On the toxicity of various commercial preparations of emetin hydrochlorid.—*Arch. Int. Med.*, 1916, xvii, 420.
A study of the buffer value of the blood.—*Ibid.*, 1916, xvii, 525.

ROWNTREE, L. G., and MACHT, D. I.

The standardization of digitals and the potency of American-grown digitals.—*J. Am. M. Ass.*, 1916, lxvi, 870.

RUSHMORE, S.

Progress in gynecology.—*Boston M. & S. J.*, 1916, clxxiv, 277; 320.
Ibid., 1916, clxxv, 494.
Treatment of weak labor pains.—*Ibid.*, 1916, clxxv, 659.

SABIN, FLORENCE R.

The origin and development of the lymphatic system.—*Johns Hopkins Hosp. Rep.*, 1916, xvii, 347.
The method of growth of the lymphatic system.—*Science*, 1916, n. s., xlv, 145; also *N. York M. J.* [etc.], 1916, ciii, 25.

SAMPSON, J. A.

The variations in the blood supply of the ovary and their possible operative importance.—*Tr. Am. Gynec. Soc.*, 1916, xli, 429.

SELLARDS, A. W.

Bacterial cultures of human spleens removed by surgical operation.—*J. Immunol.*, 1916, i, 321; also *N. Orl. M. & S. J.*, 1916-17, lxix, 502.

SELLARDS, A. W., and MINOT, G. R.

The antagonistic action of negative sera upon the Wassermann reaction.—*J. Med. Research*, 1916, xxxiv, 131.
Injection of hemoglobin in man and its relation to blood destruction, with especial reference to the anemias.—*Ibid.*, 1916, xxxiv, 469.

SELLING, L.

Benzol as a leucotoxin. Studies on the degeneration and regeneration of the blood and hematopoietic organs.—*Johns Hopkins Hosp. Rep.*, 1916, xvii, 83.

SHALLENBERGER, W. F.

Chronic urethritis in women; a new method of diagnosis in obscure urethral pain.—*J. Am. M. Ass.*, 1916, lxvi, 1011.
Some phases of nephroptosis in women.—*J. Med. Ass. Georgia*, 1915-16, v, 212.

SHARPE, W.

The cranial deformity of oxycephaly; its operative treatment, with a report of cases.—*Am. J. M. Sc.*, 1916, cli, 840.
The operative treatment of brachial plexus paralysis.—*J. Am. M. Ass.*, 1916, lxvi, 876.
Observations in the diagnosis and treatment of brain injuries in adults.—*Ibid.*, 1916, lxvi, 1536.
The results of cranial decompression in selected types of cerebral spastic paralysis due to hemorrhage.—*N. Y. State J. M.*, 1916, xvi, 475.
The operation of cranial decompression for certain intracranial conditions.—*Wisconsin M. J.*, 1916, xv, 174.

SLADEN, F. J., and WINTERNITZ, M. C.

Venous thrombosis during myocardial insufficiency.—*Johns Hopkins Hosp. Rep.*, 1916, xvii, 511.

SLEMONS, J. M.

The results of a routine study of the placenta.—*Am. J. Obst.*, 1916, lxxiv, 204.
How closely do the Wassermann reaction and the placental histology agree in the diagnosis of syphilis?—*Tr. Am. Gynec. Soc.*, 1916, xli, 363.

SLOAN, M. F.

The application of artificial pneumothorax in the treatment of pulmonary tuberculosis.—*South. M. J.*, 1916, ix, 689.

SMITH, F. J., and BARKER, L. F.,

Functional renal tests (phenolsulphonaphthalein; lactose) in orthostatic albuminuria.—*Am. J. M. Sc.*, 1916, cli, 44.

SMITH, W. H.

The educational function of the hospital.—*Mod. Hosp.*, 1916, vi, 1; also *Am. J. Nursing*, 1916, xvi, 574; *Johns Hopkins N. Alumni Mag.*, 1916, xv, 66.

A shortsighted policy on the part of hospital trustees and hospital superintendents.—*Mod. Hosp.*, 1916, vi, 268.

President's address. The American Hospital Association. *Ibid.*, 1916, vii, 312.

Hospital policy in America. Problems of the future.—*Hospital*, Lond., 1916, lxi, 63.

What is meant by hospital efficiency and some of the factors which are responsible for lack of efficiency.—*Med. Rec.*, 1916, lxxxix, 874; also *Trained Nurse*, 1916, lvii, No. 1.

STEARNS, T., WILSON, D. W., JANNEY, J. H., JR., and THURLOW, M. DE G.

Studies on parathyroid tetany.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 12.

STEVENS, A. R.

A study of extrophy of the bladder; with report of a case five years after implantation of the ureters into the rectum.—*Surg., Gynec. & Obst.*, 1916, xxiii, 702.

STRONG, R. P.

The plague of man.—*Lowell Lectures*, 1916.

STROUSE, S.

Prognosis and treatment of diabetes as influenced by recent studies.—*Illinois M. J.*, 1916, xxx, 332.

Diabetes and surgery; diabetes and pregnancy. The treatment of diabetic acidosis.—*Med. Clin.*, Chicago, 1916-17, ii, 37.

Diabetes in the young.—*Ibid.*, Chicago, 1916-17, ii, 327.

A case of renal glycosuria.—*Ibid.*, Chicago, 1916-17, ii, 339.

STROUSE, S., and FRANK, I.

The tuberculosis situation in Chicago as met by the Jewish charities.—*Associated Bull.*, Chicago, 1916 (Feb.).

Pollen extracts and vaccines in hay-fever.—*J. Am. M. Ass.*, 1916, lxvi, 712.

THAYER, W. S.

Adams-Stokes syndrome. Persistent bradycardia involving both auricles and ventricles. Remarkable prolongation of the As-Vs interval.—*Arch. Int. Med.*, 1916, xvii, 13.

Teaching and practice.—*Science*, 1916, n. s. xliii, 691; also *South. M. J.*, 1916, ix, 955; 1035.

Observations on the teaching of tuberculosis.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 92.

THEOBALD, S.

Herpes corneae "febrilis"; with special reference to etiology.—*N. York M. J.*, [etc.], 1916, civ, 247; also *Tr. Am. Ophth. Soc.*, 1916, xiv, 520.

TINKER, M. B.

What stomach symptoms justify surgical intervention.—*Delaware State M. J.*, 1916, vii, 3.

VANDERHOOF, D.

The significance of the tongue in the diagnosis of diseases of the stomach.—*Arch. Diag.*, 1916, ix, 23.

The consideration of the appetite.—*Internat. Clin.*, 1916, 26, s. ii, 22.

The fractional method of gastric analysis.—*South. M. J.*, 1916, ix, 683.

WARFIELD, L. M.

Note on an auscultatory sign over the manubrium.—*J. Am. M. Ass.*, 1916, lxvii, 1301.

WARFIELD, L. M., and KRISTJANSON, H. T.

An unusual case of so-called pseudoleukemia (Lymphosarcoma).—*Am. J. M. Sc.*, 1916, clii, 222.

WEED, L. H.

The establishment of the circulation of cerebro-spinal fluid.—[Abstr.] *Anat. Rec.*, 1916, x, 256.

WELCH, W. H.

Address to the graduating class, Johns Hopkins Hospital Training School for Nurses, Wednesday, May 24, 1916.—*Johns Hopkins N. Alumni Mag.*, 1916, xv, 140.

Medical education in the United States.—[Abstr.] *N. York M. J.* [etc.], 1916, clii, 890.

The school of hygiene and public health at the Johns Hopkins University.—*Science*, 1916, -n. s., xlii, 302.

WHIPPLE, G. H.

Protease intoxication; intestinal obstruction, peritonitis and acute pancreatitis.—*J. Am. M. Ass.*, 1916, lxvii, 15.

WHIPPLE, G. H., COOKE, J. V., and RODENBAUGH, F. H.

Intestinal obstruction. vi. A study of non-coagulable nitrogen of the blood.—*J. Exper. M.*, 1916, xxiii, 717.

WHIPPLE, G. H., and HOOPER, C. W.

Bile pigment metabolism. i. Bile pigment output and diet studies.—*Am. J. Physiol.*, 1916, xl, 332.

Bile pigment metabolism. ii. Bile pigment output influenced by diet.—*Ibid.*, 1916, xl, 349.

Icterus. A rapid change of hemoglobin to bile pigment in the pleural and peritoneal cavities.—*J. Exper. M.*, 1916, xxiii, 137.

WHIPPLE, G. H., RODENBAUGH, F. H., and KILGORE, A. R.

Intestinal obstruction. v. Protease intoxication.—*J. Exper. M.*, 1916, xxiii, 123.

WILLIAMS, J. W.

Dispensary abuse and certain problems of medical practice.—*J. Am. M. Ass.*, 1916, lxvi, 1902; also *Bull. Med. & Chir. Fac. Maryland*, 1915-16, viii, 229.

WILSON, G.

Medical education with reference to rural communities.—*J. Am. M. Ass.*, 1916, lxvi, 1073.

Disease in apparently healthy colored girls.—*New York M. J.* [etc.], 1916, clii, 585.

WINTERITZ, M. C.

Primary carcinoma of the liver.—*Johns Hopkins Hosp. Rep.*, 1916, xvii, 143.

Some observations on the effect of feeding glands of internal secretion to chicks.—*Ibid.*, 1916, xviii, 21.

Hyaline degeneration of the islands of Langerhans in pancreatic diabetes.—*Ibid.*, 1916, xviii, 37.

Generalized miliary tuberculosis resulting from extension of a tubercular pericarditis into the right auricle.—*Ibid.*, 1916, xviii, 49.

WINTERITZ, M. C., and BOGGS, T. R.

Acute suppurative hypophysitis as a complication of purulent sphenoidal sinusitis.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 56.

WINTERITZ, M. C., and SCHMEISSER, H. C.

Studies on the relation of fowl typhoid to leukemia of the fowl.—*Johns Hopkins Hosp. Rep.*, 1916, xviii, 25.

WINTERITZ, M. C., and SLADEN, F. J.

Venous thrombosis during myocardial insufficiency.—*Johns Hopkins Hospital Rep.*, 1916, xvii, 511.

WOLMAN, S., and HAMMAN, L.

Chronic non-tuberculous pulmonary infections.—*Nat. Ass. Study & Prev. Tuberc. Tr.*, 1916, xii, 171.

WOOLLEY, P. G.

Fundamentals of pathology. For students and general practitioners of medicine and dentistry, and for nurses in training schools.—St. Louis, 1916, C. V. Mosby Co., 184 p. 8°.

Gumma of the pituitary associated with lesions in the spinal cord which may represent early lesions of syringomyelia.—*J. Lab. & Clin. M.*, 1915-16, i, 155.

Carbon dioxide and blood pressure.—(Editorial.) *Ibid.*, 1915-16, i, 203.

Nervous influence and edema.—(Editorial.) *Ibid.*, 1915-16, i, 267.

Intestinal stasis.—(Editorial.) *Ibid.*, 1915-16, i, 269.

Fetal erythroblastosis: fetal erythroblastomatosis.—*Ibid.*, 1915-16, i, 347.

The pituitary in hibernation.—(Editorial.) *Ibid.*, 1915-16, i, 456.

Heteroplastic bone and bone-marrow formation associated with tuberculosis in the adrenal.—*Ibid.*, 1915-16, i, 502.

The epiphysis (The pineal gland).—(Editorial.) *Ibid.*, 1915-16, i, 527.

Cancer and X-rays.—(Editorial.) *Ibid.*, 1915-16, i, 538.

Acidosis in nephritis.—(Editorial.) *Ibid.*, 1915-16, i, 620.

Tumor problems.—(Editorial.) *Ibid.*, 1915-16, i, 625.

Diuresis.—(Editorial.) *Ibid.*, 1915-16, i, 628.

Chloroform necrosis of the liver.—(Editorial.) *Ibid.*, 1915-16, i, 630; 782.

Acidosis.—(Editorial.) *Ibid.*, 1915-16, i, 712.

The pituitary and growth.—(Editorial.) *Ibid.*, 1915-16, i, 715.

Splenectomy.—(Editorial.) *Ibid.*, 1915-16, i, 717.

Gastrointestinal diseases.—(Editorial.) *Ibid.*, 1915-16, i, 763.

The nephroses.—(Editorial.) *Ibid.*, 1915-16, i, 776.

Gastric ulcers.—(Editorial.) *Ibid.*, 1915-16, i, 928.

Edema of the lungs.—(Editorial.) *Ibid.*, 1915-16, i, 931.

The heart in pneumonia.—(Editorial.) *Ibid.*, 1915-16, i, 932.

Amyloid.—(Editorial.) *Ibid.*, 1915-16, i, 933.

Cases of infection terminating in septicemia.—*Ibid.*, 1916-17, ii, 45.

Some good autopsy figures.—*Mod. Hosp.*, 1916, vi, 377.

The autopsy room.—*Lancet-Clinic*, 1916, cxv, 313, 336, 413, 522, 564.

WOOLLEY, P. G., PEPPER, W., and BLUMER, G.

The function of the dispensary.—*J. Am. M. Ass.*, 1916, lxvi, 1156.

WOOLLEY, P. G., and MORRIS, R. S.

The clinic and autopsy room.—*Lancet-Clinic*, 1916, cxvi, 66, 89, 164, 233, 258, 398, 401, 404, 475.

YATES, J. L.

The etiology, pathology and therapy of Hodgkin's disease and allied affections.—*Colorado Med.*, 1916, xiii, 39.

YATES, J. L., and BUNTING, C. H.

Bacteriological results in chronic leukemia and pseudoleukemia.—*Stud. Rockefeller Inst. M. Research*, N. Y., 1916, xxiv, 123.

YOUNG, H. H.

Urological examining and operating table.—*Mod. Hosp.*, 1916, vi, 457.

The Witmer form board.—*Psychol. Clin.*, 1916, x, 93.

The renaissance of urology.—*South. M. J.*, 1916, ix, 146.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

OCTOBER 16, 1916.

The first meeting of The Johns Hopkins Medical Society for the season was held on October 16, with Dr. W. S. Thayer in the chair. The following officers were elected for the ensuing year: Dr. W. W. Ford, president, and Dr. C. G. Guthrie, secretary.

1. Exhibition of Cases: Cases 1, 2 and 3. DR. DANDY.

CASE 1 (Dr. Dandy).—This is a woman who had a cerebello-pontine tumor which I operated upon a month ago in Dr. Heuer's absence. She is now about ready to leave the hospital. Dr. Heuer has also two other patients, who live in the immediate vicinity and who will come before the Society to-night. Tumors were removed from both of these patients. Dr. Heuer removed one about six months ago, and the other was removed by Dr. Cushing about four years ago.

The first patient is 25 years old. Her symptoms began about one year ago with staggering gait, which gradually increased, until at the time of her admission to the hospital, she was unable to walk without support. In addition, deafness had begun in the right ear about the same time, and had also progressed, until on admission she was totally deaf on this side. She had had at times a little rigidity and tenderness in the occipital region, but nothing of any marked importance. She had also noticed a gradual diminution of vision in the left eye. A congenital cataract was present in the right eye. At times there had been attacks of amaurosis.

On admission, with the exception of a moderate grade of choked disc, there were present no signs of intracranial pressure. She had no vomiting and no headache. The symptoms suggested definitely localization in the region of the cerebellopontine angle. There was complete deafness and absence of any caloric response in the eighth nerve, with absence of bone conduction and air conduction. The Bárány test gave no response. A very slight facial weakness seemed to be present, with possibly a little weakness of the masseter muscles. There was a slight implication of the fifth and seventh nerves and a complete involvement of the eighth nerve, the syndrome of the typical endothelioma of the eighth nerve. She had most marked cerebellar signs, very marked staggering gait; in fact she could not walk alone. The Romberg test was decidedly positive. She would fall in any direction, but more to the right. She had also a very distinct nystagmus, quick to the right and slow to the left. Ataxia of the left hand was marked and there was also diadokokinesia.

The operation was done about a month ago, the usual cerebellar exploration, and an enucleable tumor was found embedded in the pons and medulla. It shelled out as a whole quite readily. She has had a perfectly uneventful recovery. Her symptoms are still marked. She has all the cerebellar symptoms and the eighth nerve involvement, but is improving very markedly day by day. She can now walk alone. The patient will, of course, continue to improve.

CASE 2 (Dr. Dandy).—This patient is a man about 50 years old, on whom I did a decompression for a perfectly unlocalizable tumor about four years ago when Dr. Cushing was away. He had nothing but the symptoms of general intracranial pressure. At the operation the tumor was found, and was removed one month later by Dr. Cushing. It was a large dural endothelioma from the right temporal lobe. After this, the patient had some weakness of the left hand, which has gradually cleared up.

CASE 3 (Dr. Dandy).—This man was operated upon by Dr. Heuer, who removed a large dural endothelioma from the pre-Rolandic region about six months ago. There is a marked con-

trast between Case 2 and Case 3. This patient, a man of 53, had no signs of intracranial pressure whatever, unless one might take a few spells of indigestion as meaning intracranial symptoms. He had absolutely no choked disc. His symptoms were a slight weakness in the left leg, which gradually involved the left arm during about one year. About a year ago when the symptoms began, he was operated upon by an outside surgeon for a deformity of the foot. This undoubtedly was due to the beginning of his pyramidal tract involvement. Looking at this patient as he walks, you can see the almost perfect result. On looking at his head, one could hardly tell he had had a cranial operation. There is only a slight depression, which is evident on looking straight at the wound. Dr. Heuer removed a good portion of the dura with the tumor, so that it could not recur. Over this defect in the dura, he placed some fascia taken from the thigh, and this has been partially responsible for the good cosmetic result. It has been six months since the operation and the patient has practically no residuum. At the time of operation, he had a very marked typical spastic hemiplegic gait, but he now shows nothing and is entirely cured.

These two cases show a very marked difference in the manifestations of intracranial tumors, both in the same region. One patient had almost entirely general and no local manifestations; the other had all local, without any general, manifestations. This is a type of tumor of which we have had a considerable number, and of which there is very little chance of recurrence. They can be permanently cured.

2. Exhibition of a Case of Gigantism In a Girl 12 Years of Age.

DR. G. J. HEUER.

K. G. Age 12, school girl. *Complaint:* Nervousness and headaches.

Family History: Both parents are living and well. The mother is rather obese but not over the normal height; the father is a tall, large man. There are eight sisters and one brother living—all apparently normal children.

Past History: The patient was born in a normal labor. Her mother states that she was a large child, weighing, she thinks, 12 pounds. She is not very clear as to the child's growth, but she thinks that the child grew faster than her other children and that her growth has been progressive and not especially rapid in the last few years. The girl herself states that she has grown rapidly in the past three years. At the age of five she had measles, and there followed a series of complications which confined her to bed for three months. There is no history of whooping-cough or diphtheria. She had chorea at the age of seven. During the attacks she was particularly bothered by twitching of the face; occasionally her whole body jerked. She was never kept out of school on account of this trouble. She has suffered from headache since the age of six, when she started to school. She has worn glasses for about six years. There has been definite shortness of breath on exertion and occasional palpitation of the heart. No edema of the extremities. No precordial pain. The appetite has been very good. The bowels have been regular. She is exceptionally fond of candy and she drinks large amounts of water. She gets up at night three or four times to void. Menstruation has not yet appeared. The breasts have just begun to enlarge. Some pubic hair has appeared in the past year.

Present Illness: The patient enters the hospital because of headaches and nervousness. The headaches began six years ago, when she first entered school. The pain begins over the left eye and radiates backward. It has been worse in the morning. The use of glasses has not improved the condition. There has never been vomiting associated with the headaches. There has been no disturbance of vision. Within the past year the girl has been

especially nervous. She cannot remain long at one occupation, has grown fidgety and restless. She has, of course, been aware of her abnormal height, but has never been troubled by it in any way. She states that she tires rather more easily on exertion than she thinks she should. She has always been slender. She is rather above the average in intelligence. At the age of 12 she is in the high school. She reads literature rather advanced for her age.

Examination: The girl is 6 feet, 1 inch in height. She weighs 117½ pounds. The skin is soft, with a tendency toward dryness rather than moisture. There is no increased wrinkling of the skin. The hair is fine. There is some fullness of the frontal bosses. The biparietal diameter of the skull is not great. The head is not long anteroposteriorly. The nose is a little wide, but not abnormally large. The jaw is not especially over-developed. The teeth meet accurately; if anything, the lower teeth fall behind the upper. The extremities are abnormally long; the hands and feet very large, but there are no acromegalic features. Examination of her cranial nerves shows no disturbances. The fundi are normal. The visual fields show a defect in the upper outer quadrant of each visual field, suggesting a beginning bitemporal hemianopsia. The neurological examination is otherwise quite negative. The X-ray of the skull shows an enlarged sella turcica, with atrophy of the posterior clinoid processes.

Thyroid: The isthmus is just palpable. Neither lobe can be definitely felt. There is no enlargement of the neck. No dullness behind the manubrium on percussion. No signs indicative of hyper- or hypothyroidism.

Adrenals: No abnormal pigmentation of the body. No pigmentation of the mucous membranes. No abdominal masses felt. There is considerable spasticity of the sigmoid.

Ovaries: A gynecological examination has not been made. On abdominal palpation nothing abnormal is made out. Menstruation has not begun.

Pineal Gland: Nothing abnormal is noted.

Laboratory Findings: Urine: There is a history of abnormal thirst. The patient rises three or four times at night to void. The average daily output of urine is 1500 cc. The average intake of water about 2000 cc. Three specimens of urine have shown a slight trace of albumin. Sugar has never been present. The specific gravity has varied between 1007 and 1013. The chlorides have been decreased.

Blood: Hemoglobin 71%. Polymorphonuclear neutrophils, 61.2%; large mononuclears, 10.4%; small mononuclears, 22.4%.

Sugar Tolerance Test: One hundred grams of glucose given upon an empty stomach cause a hypoglycemia. Half an hour after the administration of 100 grams of glucose the blood sugar was the same as that of the control, that is, .95%; 1½ hours later it fell to .67%; 2 hours later to .63%.

The pharmacodynamic tests, *i. e.*, the responses to adrenalin and atropin, are normal.

(The pulse has been about 90. The temperature was slightly elevated on admission, but has since tended to be subnormal.)

DISCUSSION.

DR. BARKER: One interesting point about the reason why the extremities grow long might be brought out. Dr. Heuer spoke of the fact that this is the kind of gigantism which occurs before puberty. The explanation assigned is this. When the external secretion of the gonads begins at puberty, it causes the closure of the epiphyses. As long as they are not closed the long bones can grow and acromegaly does not appear. This is a most interesting example of this type.

DR. THAYER: We have had a certain number of cases of this type, have we not?

DR. HEUER: Yes, but never such a pure example.

DR. THAYER: I remember one such case we had here nearly 20 years ago at least, a most interesting case of a man who had in addition an arthritis. He had these very long, tapering fingers, was very tall and had none of the ordinary stigmata of acromegaly. We had no X-rays then for detailed examinations. The case was recorded as one of acromegaly occurring before the age of puberty.

3. Action of Opium Alkaloids on the Ducts of the Testis. DR. DAVID I. MACHT.

Following the author's experiments on the action of drugs on the ureter, which were first announced in this journal (Bull. Johns Hopkins Hosp., 1916, XXVII, 119), attention was logically directed to the behavior of the vas deferens and seminal vesicle, which anatomically is only a diverticulum of the vas. The organs of the rabbit, guinea-pig, rat, cat, dog, sheep, and bull were utilized. The action of opium alkaloids distinguishes two groups. Those of the phenanthrene group, of which morphin and codein are the chief representatives, cause increase in tonicity and stimulation of contractions, of the vas deferens, ejaculatory duct, and seminal vesicle. Those of the isoquinoline group, of which papaverin and narcotin are the principal members, relax the tone and inhibit the contractions of the same organs. In a combination of all the opium alkaloids such as pantopon, the narcotin-papaverin effect on smooth muscle predominates. These results were, as far as possible, checked up with observations on the organs *in situ* (rabbits and guinea-pigs) and were found to hold good in the intact animal. The above observations are of some practical interest.

4. Studies on the Physiology of Thyroid Secretion (Abstract).¹ ROBERT L. LEVY, M. D.

The recent work of Cannon and Cattell has placed the secretory innervation of the thyroid gland on a firm basis. These observers have employed as their criterion of secretory activity the electrical change giving rise to the current of action. They have demonstrated that an action current is produced in the thyroid by stimulation of the cervical sympathetic nerve or by the injection of minute amounts of the sympathicomimetic substance, adrenin. The gland secretes promptly on stimulation, *i. e.*, an action current is obtained after a latent period of only a few seconds. No evidence of secretory activity is observed on stimulation of the vagus nerves, nor is there any electrical change after injection of the vagotropic drug, pilocarpine.

As a result of these studies, two methods are at hand for inducing secretory activity in the thyroid gland. It is the object of the present communication to present evidence of the presence of thyroid secretion in the circulating blood after stimulation of the cervical sympathetic nerves or after injection of adrenin and to demonstrate that thyroid secretion increases the effectiveness of adrenin in raising arterial pressure. Its effects on blood pressure and pulse rate are also recorded.

The results of the experiments may be summed up as follows:

1. In cats, after stimulation of the cervical sympathetic in the neck, there can be demonstrated an increase of the effectiveness of adrenin in raising arterial pressure. This increase may be as much as 200 to 300 per cent.
2. Injections of adrenin, even in minute amounts, produce a similar effect.
3. This effect is manifest only after a latent period, which may vary from about 40 to 60 minutes. There is then a progressive increase in the height of the curves, the maximum being reached

¹ These studies were carried out in the laboratory of physiology in the Harvard Medical School. It is a pleasure to acknowledge my indebtedness to Dr. W. B. Cannon for much helpful advice. The work is reported in full in the Amer. Jour. of Physiol., 1916, XLI, 492.

in from two to three hours after stimulation. The effect is of considerable duration, having been observed for as long as seven hours.

4. When the thyroid glands have been previously removed, cervical sympathetic stimulation or adrenin injection does not produce an increase in the pressor response to adrenin. It is therefore justifiable to conclude that (a) stimulation of the cervical sympathetic or adrenin injection induces secretory activity in the thyroid gland (thus confirming the observations of Cannon and Cattell); and (b) thyroid secretion renders more excitable the sympathetic structures acted on by adrenin in raising arterial pressure.

5. Stimulation of the cervical sympathetic causes the thyroid to secrete promptly, since thyroidectomy immediately after stimulation is followed by a progressive augmentation in pressor response similar to that observed when the glands are left in the animal throughout the course of the experiment.

6. Intravenous injection into thyroidectomized cats of a solution of the crystalline, iodine-containing compound isolated from the thyroid by Kendall, is followed by an increase in the efficacy of adrenin as a pressor agent. The effect is demonstrable almost immediately after injection and is of relatively shorter duration than in the stimulation experiments. This substance causes no appreciable alteration in blood pressure or pulse rate.

7. Neither during nor after stimulation of the thyroid gland through its secretory nerves is there any significant change in blood pressure or pulse rate.

8. After thyroid stimulation, even at the time when adrenin is more effective as a pressor agent, there is no increase in the augmentation of pulse rate produced by adrenin injection. This

indicates a selective action of thyroid secretion in sensitizing sympathetic tissues to the action of adrenin, since the increase in vascular response is not associated with greater excitability of the augmentors of the heart.

9. In cats whose adrenal glands have been previously removed, there can be demonstrated, after thyroid stimulation, an increase in pressor response similar to that seen in unoperated animals. Though there is some evidence in the literature indicating that thyroid secretion acts as a secretory stimulant to the adrenals, the increased effectiveness of adrenin as a pressor agent after thyroid stimulation is not dependent on a greater amount of circulating adrenin.

5. Some Results of Plastic Surgery. DR. J. S. DAVIS.

Dr. Davis presented a series of lantern slides, showing some of the results he had obtained in cases requiring plastic operations. Interesting pictures were shown of cases of severe burns of the hands, with subsequent loss of flexion or extension, which were restored to usefulness. Good cosmetic and functional results were shown following plastic operations and whole thickness skin grafting in cases of ectropion of the eyelids, and eversion of the lower lip. Other cases included the formation of a cheek after destruction of tissue following removal of a sarcoma; the formation of an ear to replace one lost by trauma; the filling in of the orbit with a pad of fat and skin, following enucleation of the eye with removal of the eyelids; relief of contracture of the axilla following a burn; the correction of saddle nose with a free cartilage transplant. In each instance the patient was much improved both as to function and appearance.

BOOKS RECEIVED.

A Text-Book of Pathology. By W. G. MacCallum. With 575 illustrations, chiefly from drawings by Alfred Feinberg. 1916. 8°. 1085 pages. W. B. Saunders Company, Philadelphia and London.

A Text-Book of Practical Gynecology. For Practitioners and Students. By D. Tod Gilliam, M. D., and Earl M. Gilliam, M. D. Fifth revised edition. Illustrated with 250 engravings, a colored frontispiece, and 13 full-page half-tone plates. 1916. 8°. 681 pages. F. A. Davis Company, Philadelphia; Stanley Phillips, London.

Practical Massage and Corrective Exercises. By Hartvig Nissen. Revised and enlarged edition of the author's "Practical Massage in Twenty Lessons"; with many additions. With 68 original illustrations, including several full-page half-tone plates. 1916. 12°. 211 pages. F. A. Davis Company, Philadelphia; Stanley Phillips, London.

Venesection. A Brief Summary of the Practical Value of Venesection in Disease. For Students and Practitioners of Medicine. By Walton Forest Dutton, M. D. Illustrated with several text engravings and three full-page plates, one in colors. 1916. 8°. 221 pages. F. A. Davis Company, Philadelphia; Stanley Phillips, London.

Christianity and Sex Problems. By Hugh Northcote, M. A. Second edition. Revised and enlarged. 1916. 8°. 478 pages. F. A. Davis Company, Philadelphia; Stanley Phillips, London.

The Non-Surgical Treatment of Intestinal Stasis and Constipation. Compiled by Robert H. Ferguson, M. D., Sc. D. Also an important announcement regarding liquid petrolatum. 1916. 12°. 109 pages. E. R. Squibb & Sons, New York.

Metropolitan Asylums Board. Annual report for the year 1915. (18th year of issue.) 1916. 8°. 61 pages. Printed by Henderson & Spalding, London.

The Johns Hopkins Hospital Reports. Vol. XVIII, Fasciculus 1. Annual Report of the Department of Pathology of the Johns Hopkins University and Hospital. No. 1. 1916. 4°. 102 pages. The Johns Hopkins Press, Baltimore.

The Treatment of Infantile Paralysis. By Robert W. Lovett, M. D. With 113 illustrations. 1916. 8°. 163 pages. P. Blakiston's Son & Co., Philadelphia.

Nursing Problems and Obligations. By Sara E. Parsons, R. N. 1916. 12°. 149 pages. Whitcomb & Barrows, Boston.

Diagnosis and Treatment of Surgical Diseases of the Spinal Cord and Its Membranes. By Charles A. Elsberg, M. D., F. A. C. S. With 158 illustrations, three of them in colors. 1916. 4°. 330 pages. W. B. Saunders Company, Philadelphia and London.

Roentgenographic Diagnosis of Dental Infection in Systemic Diseases. By Sinclair Tousey, A. M., M. D. 1916. 8°. 75 pages. Paul B. Hoeber, New York.

The Medical Clinics of Chicago. Vol. II, No. 1, July, 1916. 1916. 8°. 220 pages. W. B. Saunders Company, Philadelphia and London.

The Treatment of Diabetes Mellitus. With Observations upon the Disease Based upon 1000 Cases. By Elliott P. Joslin, M. D. Illustrated. 1916. 8°. 440 pages. Lea & Febiger, Philadelphia and New York.

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TRANSFUSION OF BLOOD.

HISTORY, METHODS, DANGERS, PRELIMINARY TESTS, PRESENT STATUS. REPORT OF ONE HUNDRED AND FIFTY TRANSFUSIONS.

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AND

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(From the Surgical Clinic of the Johns Hopkins Hospital.)

From the very earliest times, the blood has been regarded as synonymous with life. It was considered by the ancients as the seat of the soul. In the Bible¹ we have the following: "Because the life of the flesh is in the blood and I have given it to you upon the altar to make an atonement for your souls: for it is the blood that maketh an atonement for the soul." Many references are made to transfusion of blood in the writings of the ancient Egyptians. It was condemned by Pliny and Celsus. In the *Metamorphoses* of Ovid² we have: "Quid nunc dubitatis inertes? Stringite, ait, gladios; veteremque haurite cruorem, ut repleam vacuas juvenili sanguine venas." "Why, now, do ye hesitate and do nothing? Unsheathe your swords and draw out the old blood, that I may fill the empty veins with the blood of the youth." Libavius in 1615 reports in "*Defensione Syntagmatis arcanorum chymicorum*" as follows: "Let there be present a robust, healthy youth full of lively blood. Let there come one exhausted in strength, weak, enervated, scarcely breathing. Let the master of the art [the operator] have silver tubes that can be adapted one to the other; then let him open an artery of the healthy one, insert the tube and secure it. Next let

him incise the artery of the patient and put into it the feminine [receiving] tube. Now let him adapt the two tubes to each other and the arterial blood of the healthy one, warm and full of spirit, will leap into the [vessels of the] sick one, and immediately will bring to him the fountain of life and will drive away all languor."

It is recorded that Jean Baptiste Denys³ of Montpellier, physician to Louis XIV, performed the first transfusion of blood in man. In June, 1667, he injected the blood of a calf or a lamb into the veins of a young man dying from repeated venesections. The patient survived and apparently recovered his health. Violent controversies arose regarding the operation, and it was decreed that for the future no transfusion should be made on the human body except with the approbation of the physicians of the Faculty of Paris.

One hundred and seventy-five years earlier than this, however, there is a report of the transfusion of Pope Innocent VIII. The following is copied from Villari's *Life of Savonarola*:⁴ "The vital powers of Innocent VIII rapidly gave way. He had for some time fallen into a kind of somnolency, which was sometimes so profound that the whole court be-

lieved him to be dead. All means to awaken the exhausted vitality had been resorted to in vain, when a Jew doctor proposed to do so by the transfusion, by means of a new instrument, of the blood of a young person; an experiment which hitherto had been made only on animals. Accordingly, the blood of the decrepit old Pontiff was passed into the veins of a youth, whose blood was transferred into those of the old man. The experiment was tried three times, and at the cost of the lives of three boys, probably from air getting into their veins, but without any effect to save that of the Pope. He expired on the 25th of April, 1492." However, another version, contradicting the above is found in "The Life and Times of Rodrigo Borgia:" "Three boys were bled until they died, and the Pope drank a draught prepared from this blood, without benefit." It seems probable that transfusions of blood were attempted before the time of Harvey's discovery of the circulation of the blood in the 17th century.

In the diary of Samuel Pepys we read:

"November 14, 1666, Dr. Croone told me, that, at the meeting at Gresham College tonight, which, it seems, they now have every Wednesday again, there was a pretty experiment of the blood on one dogg let out till he died into the body of another on one side, while all his own ran out on the other side. The first died upon the place. The other very well, and likely to do very well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but, as Dr. Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body."

In a footnote the following:

"At the meeting on November 14th, the experiment of transfusing blood of one dog into another was made before the Society by Mr. King and Mr. Thomas Coxe upon a little mastiff and a spaniel with very good success, the former bleeding to death, and the latter receiving the blood of the other, and emitting so much of his own as to make him capable of receiving that of the other."

On November 21st the spaniel "was produced and found very well." The experiment of transfusions of blood which occupied much of the attention of the Royal Society in its early days has been revived within the last few years.

"November 16. This noon I met with Mr. Hooke, and he tells me the dog which was filled with another dog's blood, at the College the other day, is very well, and like to be so as ever, and doubts not its being found of great use to men; and so to Dr. Whistler, who dined with us at the tavern."

Denys reports several transfusions, from 5 to 10 ounces of arterial blood of a lamb being usually employed; the first, the depletion from the venesection case, with complete cure; the second purely experimental, a perfectly healthy man agreeing to the trial. Ten ounces of blood were removed from his vein and a similar amount from a lamb was injected into him. No disagreeable results were noted, and the man experienced an agreeable sensation of warmth. The third case was in a man, 34 years old, who had escaped from a place of confinement, having been insane for eight years. He was captured and transfused by Denys with five or six ounces of blood from a calf. As soon as he became calm a larger quantity was used. The disapprobation of the Faculty of Paris discouraged further transfusions in France until early in the 19th century.

About the time that Denys was working in France, Lower³ was carrying on similar experiments in England. He reports his discoveries beginning with the year 1683, though before this, as far back as 1666, he had transfused the blood of three calves into three dogs. One of the dogs "from which so much blood had been drawn the day before that he could hardly stir any more, having been supplied the next morning with the blood of a calf, recovered instantly his strength and showed a surprising vigor."

This is the method of transfusion described by Dr. Lower:

"First take up the Carotidal Artery of the Dog or other Animal, whose blood is to be transfused into another of the same or different Kind, and separate it from the Nerve of the 8th Pair, and lay it bare above an Inch. Then make a strong ligature on the upper Part of the Artery not to be untied again: But an Inch below, viz. towards the Heart, make another Ligature of a running Knot, which may be loosened or fastened as there shall be Occasion. Having made these two Knots, draw two Threads under the Artery between the two Ligatures: and then open the artery, and put in a quill, and tie the Artery upon the Quill very fast by those two Threads, and stop the Quill with a Stick. After this, make bare the Jugular Vein, in the other Dog, about an Inch and a Half long: and at each End make a Ligature with a running Knot, and in the Space between the two running Knots draw under the Vein two Threads as in the other: Then make an Incision in the Vein, and put into it two Quills, one into the descendent Part of the Vein, to receive the Blood from the other Dog, and carry it to the Heart: and the other Quill put into the other Part of the Jugular Vein (Which comes from the Head) out of which the second Dog's own Blood must run in the Dishes. These two Quills being put in and tied fast, stop them with a Stick, till there be occasion to open them. All Things being thus prepared, fasten the Dogs on their Sides towards one another so conveniently that the Quills may go into each other. After that unstop the Quill that goes down into the first Dog's Jugular Vein, and the other Quill coming out of the other Dog's Artery; and by the help of two or three other Quills, put into each other, according as there shall be occasion, insert them into one another. Then slip the running Knots, and immediately the Blood runs through the Quills, as through an Artery, very impetuously. And immediately, as the Blood runs into the Dog, unstop the other Quills, coming out of the upper Part of his Jugular Vein (a Ligature being first made about his Neck, or else his other Jugular Vein being compressed by one's Finger) and let his own blood run out at the same Time into Dishes (not constantly, but according as you perceive him able to bear it) till the other Dog begins to cry, and faint, and fall into Convulsions, and at last die by his Side.

"Then take out both Quills out of the Dog's Jugular Vein, and tie the running Knot fast, and cut the Vein asunder (which you may do without any Harm to the Dog, one Jugular Vein being sufficient to convey all the Blood from the Head and upper Parts, by reason of a large Anastomosis, whereby both the Jugular Veins meet the Larynx.) This done, sew up the Skin, and dismiss him, and the Dog will leap from the Table, and shake himself, and run away as if nothing ailed him.

"Or, instead of a Quill, take a small crooked Pipe of Silver or Brass, so slender that one End may enter into a Quill; and having at the other End, that is to enter into the Vein and Artery, a small Knob, and for the better fastening them to it with a Thread; for this is much more easy to be managed than a Quill."

There is much interesting material in this article by Dr. Lower. For instance, he reports the cure of a mangy dog in ten days after transfusions with blood from a healthy dog.

He reports the transfusion of a dog for acute anemia following splenectomy with hemorrhage. He cites a letter from M. Denys from Paris concerning the transfusion of a 26-year-old horse with the blood of four wethers. Many transfusions were done from one species to another.

He reports in detail the experiment of transfusing the blood into human veins by Dr. Arthur Coga, November 23, 1667. The patient was bled seven ounces and then joined to the artery of a sheep by means of the Lower "pipe." The transfusion continued two minutes. It was estimated that 9 or 10 ounces were received into the man's veins. "The man, after the operation as well as in it, found himself very well."

He also reports experiments with non-coagulates, such as spirits of sal ammoniac. Dr. Lower died in 1691. His experiments were repeated by Sir Edmund King, Thomas Coxe, Gayant and Denys.

Then followed a long interval during which transfusion appears to have fallen into disrepute. During the Franco-Prussian War and afterward transfusion was in vogue, but was again given up. Between 1850 and 1875 many transfusion experiments were being carried on in the physiological laboratory of Greifswald. Leisrink was also working with transfusion in Hamburg. The work in Greifswald was being done by Eulenburg and Landois. The latter devised an apparatus for the direct transfusion of blood from the vein of the donor to the vein of the recipient by means of cannulas and tubing. In 1875 he published his monograph, "Die Transfusion des Blutes."

In this country the first article which we found was by Dr. William S. Halsted.⁷ He reports several cases of carbon-monoxide poisoning treated by transfusion or refusion of blood. He first drew the blood, defibrinated it, and then re-injected it into the patient. "Refusion of blood is literally a depletory transfusion in which the blood withdrawn is returned to the circulation of the loser."

As to the best methods of infusing fluids into the circulation good authorities disagree. Of the four possible methods, centrifugally or centripetally into an artery or vein, the question of centrifugal venous infusion is mentioned only to be discarded. Hueter, who gives to von Graefe the honor of being the first to draw attention to centrifugal arterial transfusion, deserves the credit of having introduced it to the profession and strongly advocated the method. Kümmell, Schede's assistant, produced gangrene of the hand by the centrifugal infusion of a saline solution into the radial artery. Hueter's arguments for peripheral or centrifugal arterial transfusion are, that the blood courses more slowly and more uniformly to the heart and the danger of phlebitis is avoided. Landois adds to these advantages another—that the capillary system, like a supplementary filter, catches all foreign articles which may be present. Dr. Halsted advocated the centripetal arterial infusion, since the above arguments hold good for centripetal as well as centrifugal arterial transfusion.

The syringe method of transfusion which we have been using for the past year was perfected by Lindeman.⁸ The first report made on it was in 1892 by Prof. von Ziemssen.⁹ Von Ziemssen at first injected whole blood subcutaneously, and used vigorous massage for 15 minutes. The procedure was very painful, since he used 300 to 450 cc. of blood at an injection. The hemoglobin was increased by 10 to 15 per cent and von Ziemssen reports that there was no fever and no hemoglobinuria in these cases. Next he devised the method of syringes. He inserted a needle into the vein, withdrew a syringe full of blood and injected it through a needle already inserted into the vein of the recipient. He advised at least three syringes of a capacity of 25 cc., so that while one was being filled and one being emptied, the other one could be cleaned out with sterile salt solution. Following the intravenous infusion he occasionally noted a rise of temperature and chill, but in no case was there hemoglobinuria. There was no evidence of hemolysis, and no free hemoglobin was found in the blood serum. He encountered no phlebitis or secondary thrombosis and he found that the needle could be stuck into the vein again at the same place. He always had a number of needles ready. His average transfusion was from 200 to 300 cc. Von Ziemssen first raised the question whether often repeated transfusions in the bad progressive anemias might have a use, and suggested the possibility that by these means a real cure might result in some of these cases. He reports one case of anemia in a woman, 38 years old, whom he transfused seven times with marked benefit each time and a rise in the hemoglobin. He experimented on the relative value of blood transfusions and saline infusions and concluded that the salt infusion was of benefit only for a short time.

The next great steps were made in this country chiefly in the line of simplifying the technique and making more sure of success in transferring a sufficient quantity of blood from the donor to the recipient. The work of Carrel¹⁰ on the direct successful end-to-end suture of blood vessels (as well as the cannula devised by Crile),¹¹ added a new interest. Before this time, excepting for the work of von Ziemssen, one could not be certain that any blood would enter the veins of the recipient. During the past few years multitudes of cannulas and methods of suture have been devised. These newer methods have made safe the transfer of blood without the former danger of clotting and subsequent embolism.

BRIEF REPORT OF SUTURES AND CANNULAS.

Carrel's success, as you know, was due mainly to the most rigid aseptic technique and the prevention of blood clotting in the wound, or in the severed blood vessels during the operation, by means of careful hemostasis and saline irrigation. His manual dexterity, fine needles and suture materials and exact approximation of intima and media, were also important factors. Then came the Crile cannula with the principle of everting one vessel over a hollow cylinder and inserting this into the recipient vessel. In this method the intima coats are brought together and there are no raw surfaces. Follow-

ing this there came a number of imitations with improvements, the best of these being the Elsberg¹² cannula. Sauerbruch¹³ and Hartwell¹⁴ devised a method of slipping the ends of the artery directly into the end of the vein. This was fairly successful. Levin,¹⁵ Janeway,¹⁶ Soresi¹⁷ and McGrath¹⁸ employed methods more or less similar, the vessels being everted over hollow cylinders and then brought together directly end-on, by sliding the two parts on a little track or by closing a clamp.

The main objection to all of these methods is that they cause a considerable amount of inconvenience to both donor and recipient. The amount of blood cannot be determined absolutely excepting, perhaps, by methods suggested by Libman and Ottenberg.¹⁹ Oftentimes the artery would go into a spasm from which it would not recover for half an hour or more, so that only a very small quantity of blood could pass through. This spasm sometimes could be overcome by irrigations of hot salt solution.

Then came the indirect methods, that is, methods in which the blood, while being transferred, comes in contact with the walls of the cannula, a receptacle, a needle or a syringe. The first of these was carried out in London in 1666 by Dr. Lower; the first from man to man in France by Denys, who used quills described above. Landois,²⁰ about 1860, used the rubber tubes. These methods were probably unsatisfactory. In 1909 Brewer and Leggett²¹ used simple glass tubes coated with paraffin extending from the vessel of the donor to the vessel of the recipient. This proved to be a very efficient method. Pope²² modified it somewhat by using a rubber tube between two glass cannulas. Bernheim²³ used the silver cannula, one-half being fitted into the artery of the donor, the other into the vein of the recipient—one cannula then fits into the other, completing the connection.

BLOOD WITHDRAWN AND REINJECTED.

For the prevention of clotting most of these methods, for instance, those of Curtis and David²⁴ (1911), depend upon paraffin-coated receptacles. Kimpton and Brown,²⁵ Satterlee and Hooper,²⁶ and Percy,²⁷ developed methods for measuring the blood and then reinjecting it. In none of these was there at first an addition of any foreign element. The best of these methods is apparently that devised by Kimpton and Brown: the blood can be withdrawn in one room and taken into another for injection into the recipient.

The greatest advance that has been made in solving the technical difficulties of transfusion came with the introduction of the syringe method. It is so easy and so simple, causing no inconvenience to either donor or recipient, that it is almost an ideal method. Whether ultimately only one syringe or several will be used is yet to be determined. The syringe method²⁸ * was first described and used by Prof. H. von Ziemssen, Director of the Medical Clinic in Munich, in 1892.⁹

* Blundell (1818) was probably the first man to use the syringe in transfusion, although since he employed only one syringe, he could not transfer very large quantities of blood.

He used a number of needles which were put directly into the veins of recipient and donor. He advised at least three syringes of 25 cc. and two or three assistants. The syringe was filled with blood from the donor, which was then injected directly into the recipient. While this injection was being made, the second syringe was being filled. When the first syringe was emptied of its blood it was immediately washed out with normal salt solution by an assistant, so that a continuous transfusion was going on. He reports a number of cases treated by this method, the average transfusion being about 300 cc.

On April 10, 1913, before the New York Academy of Medicine, Lindeman reported an elaboration of this method by the use of improved needles and more syringes. Von Ziemssen's method had been practically forgotten and Lindeman's revival was apparently a great advance.

Recently there have been invented several devices by means of which only one syringe is used, as in that of Watts (not reported) in Dr. Halsted's Clinic, and in those of Kush,²⁹ Bernheim,³⁰ Cooley and Vaughan,³¹ and then later of Unger³² in New York. The Unger apparatus is probably the best. A continuous injection of salt solution is made through the apparatus so that the blood does not have time to clot in it. The syringe is kept cool by means of an ether spray which retards clotting. There is but little danger of any infection being carried from recipient to donor.

HERUDIN AND SODIUM CITRATE, PLASMAPHÆRESIS METHODS.

At the same time that work was being done to find a mechanical way of preventing clotting, that is, a more rapid or more perfect way of transferring the blood, investigators were turning their attention to the chemical side of the problem with the hope that if the blood could be kept from clotting by means of some chemical, the difficulty of transfusion would be immediately solved. The two chemicals most used have been herudin and sodium citrate. Prof. John Abel³³ has done a great amount of work along the line which has led up to his plasmaphæresis method, and we have tried this in one patient with uremia in this hospital.

Blood was withdrawn from the patient into receptacles containing herudin. These receptacles were taken for some distance to the laboratory. The red corpuscles were separated from the plasma, then brought back to the operating room and reinjected into the patient in normal salt solution.

Satterlee and Hooper in New York during 1914 reported favorably on the herudin method. The sodium citrate method was reported by three workers almost simultaneously; first, however, by Hustin,³⁴ from Brussels, a little later in this country by Weil³⁵ and then by Lewisohn³⁶—each publishing his article early in 1915. These methods have proved very successful and have the advantage that blood may be kept for some time, even four or five days, on ice and then be injected into the recipient.

At first the objection was made that the use of any drug to delay coagulation time would contra-indicate the transfusion, since in a great many cases in which transfusion is indicated there is already bleeding with increased coagulation

time. With oxalate and citrate solutions the calcium of the blood is fixed, and the calcium is a necessary factor in spontaneous coagulation. Practice with the method, however, apparently has shown that the coagulation time of the recipient is not lengthened but is actually shortened. This is hard to explain.

Defibrinated Blood.—The syringe method and the citrate method of transfusion appear to us to have forever abolished any justification for the injection of defibrinated blood, although this procedure has saved lives and done a great deal of good. The reaction, however, with chill and high fever after the injection of defibrinated blood in so many cases would indicate that the method should be given up.

The work of Dr. Halsted in 1882, and that of Dr. Moss³⁷ with defibrinated blood should not be forgotten. Dr. Halsted concluded from his work with the cases of gas poisoning that the depletion and not the refusion was the more beneficial.

Hemolysis.—If the mechanical difficulties had been the only ones to be overcome, we are sure that transfusion would now have a far different standing in the medical world. Discredit must have repeatedly been thrown on the procedure by the accidents, often fatal, due to hemolysis. It was Landois who first showed that the serum of one animal may have the property of destroying the red blood cells in another. Hayem³⁸ reported that in a transfusion from an ox to a dog, a serious condition resulted, resembling purpura hemorrhagica, death occurring in a few hours. He says: "The effect of a foreign cell on the circulating blood is such that the latter immediately becomes finely clotted and carries the thousands of clots into the small vessels, and one sees innumerable infarcts formed." In the present paper we shall not discuss the development of knowledge along these lines and the serological tests which have become so essential.

Eight or nine years ago, great discredit was thrown upon these laboratory tests by most of the men doing transfusion. It was the common saying that hemolysis or agglutination might occur *in vitro* but not *in vivo* and vice versa. At first I agreed with this attitude and, while in New York,³⁹ good fortune was on my side and I had no serious accidents. Later, however, I became convinced of the great importance of these tests and shall never again consent to do a transfusion except under the most extreme urgency without the proper report from these laboratory tests. The fault, at first, probably was due to the fact that the tests were not allowed to run long enough. We firmly believe now that they should be negative at the end of one hour—never less—or, if possible, after a longer observation. All diseases transmissible by transfusion must be carefully ruled out by careful and accurate examinations.

Transfusion has been tried in the following conditions: pernicious anemia, illuminating-gas poisoning, exophthalmic goitre, hemophilia, toxemia, shock, hemorrhage, leukemia, septicemia, purpura hemorrhagica, malnutrition, endocarditis, intoxication, general debility, dysentery, typhoid fever, infectious diseases, melena neonatorum, scarlet fever, pellagra, tuberculosis and tumors. It has also been used for vaccinating purposes.

The best results have been obtained in hemophiliacs and babies with melena neonatorum; in the latter it is a specific, and in the former it stops the bleeding immediately, although without curing the disease. It is of great benefit in all anemias and with proper regulation may be of still more benefit in the primary types. Thus far, in shock it has been disappointing. This may very well be due to the fact that the shock has progressed too far before the transfusion has been done. We would advise a very early transfusion in cases of shock.

Following acute and prolonged hemorrhages transfusion is of the greatest benefit. For gas poisoning, bleeding is beneficial, as was pointed out by Halsted. Depletion followed by injections of saline solution is as good, if not better, than transfusion. In tuberculosis there has been only slight benefit and, so far, nothing has been accomplished by transfusion in malignant diseases in man.

Vaccinating Transfusion.—There is a great field still to be developed along these lines. Our experiences in typhoid fever have been very satisfactory. It would be very desirable to have a series of donors who have recently had typhoid fever ready to give blood to very ill typhoid patients. In one patient, depleted by hemorrhages as well as having a high-grade toxemia, the transfusion of blood, from a person who had previously had typhoid fever, brought about the most marked improvement, the temperature dropping to normal and the hemorrhage ceasing, with a temporary disappearance of the toxemia. This is very suggestive of the good that might be accomplished by transfusing typhoid fever patients with blood from patients who have recently had the disease and who have probably a high grade of immunity. It would be interesting to try this type of transfusion in patients with other diseases and the procedure might prove very beneficial.

REPORT OF OUR TRANSFUSIONS.

We have done 150 transfusions for 80 patients, as shown in the following table:

Groups of Cases.	Cases.	Transfusions.
1. Pernicious Anemia ^{40*}	17	64
2. Secondary Anemia	19	23
3. Hemophilia	2	5
4. Shock	2	2
5. Hemorrhage	6	6
6. Leukemia	5	6
7. Intoxications	7	9
8. Septicemia	3	11
9. Dysentery	1	1
10. Typhoid Fever	4	6
11. Other Infections	5	5
12. Purpura Hemorrhagica	1	1
13. Benzol Poisoning	3	8
14. Tumors (Carcinoma)	5	5
	80	152
Not successful (early days, direct method)	2	2
	78	150

* McClure, Roy D.: Pernicious Anemia Treated by Splenectomy and Systematic Often-Repeated Transfusion of Blood. Transfusion in Benzol Poisoning. J. Am. M. Ass., Sept. 9, 1916.

The reactions from the transfusions are shown in the following table. One death was surely due to the transfusion as an immediate cause, owing to the improper matching of the blood.

SUMMARY.

Reaction.	In Transfusions.	Per Cent.
Severe Reaction	20	13½
Slight Reaction	25	16⅔
Chill	15	10
Dilated Heart	2	1⅓
Jaundice	1	⅔
Hemoglobinuria	4	2⅔
Temp. Elevation of over 101° F... 34		22⅔
Skin Eruptions	8	5⅓
Agglutination	6	4
Hemolysis	8	5⅓
Results.		
Life Saving	15	10
Beneficial	63	42
No benefit	56	37⅓
Harmful	16	10%
Not successful. Omitted from calculations (early days, direct method)	2	100.0

152

(Two deaths probably due to transfusion, or 1⅓%; certainly one death.)

ing 5 cc. of salt solution, and immediately shaken to distribute the cells. If the patient's blood count is low, more drops are taken—i. e., if the count is 1,000,000, take five drops instead of one.

N. B.—Specimens 1 and 2 are obtained from the patient and from each prospective donor.

3. *Carrying Out the Test.*—(a) As soon as set up, the preparations should be examined to see that the suspension is uniform. The proper thickness is about that of a well-spread blood film—the cells should be close together but not clumped.

(b) Examine at the end of ten minutes. If clumping has occurred in either preparation, the bloods belong to different groups and are incompatible. If no clumping has occurred, then:

(c) Incubate at 37° C. for *one hour*.

(d) Read tests. If clumping has occurred, the bloods belong to different groups and are incompatible. If no clumping in either preparation—the bloods belong to the same group and are compatible.

In the patients for whom many transfusions have had to be done it has been observed that it is more and more difficult to find donors whose blood will match that of the patient. A donor may match perfectly early in the series of transfusions and later be found to be unsuitable. This is probably due to

	Number of Cases.	Number of Transfusions.	Severe Reactions.	Slight Reactions.	Chill.	Dilated Heart.	Jaundice.	Hemoglobi-nuria.	Temperature Elevation over 101°.	Skin Eruption.	Agglutination.	Hemolysis.	Life Saving.	Beneficial.	No Benefit.	Harmful.	Unsuccessful.	Death.
Pernicious anemia	17	64	7-10%	12-19% †	7-10%	1 (24 hrs. after trans.) -1½ % †	1-1¼ % †	3-4½ % †	12-19% †	7-10%	0	0	0	34-53%	23-35%	7-10%	0	0
Secondary anemia.....	19	23	5	3	2	0	0	1	8	0	2*	2*	2	10	5	4	2	1
Hemophilia.....	2	5	0	0	0	0	0	0	0	0	0	0	4	0	1	0	0	0
Shock	2	2	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
Hemorrhage	6	6	1	0	1	0	0	0	1	0	1 (?)	1 (?)	0	2	3	1	0	0
Leukemia.....	5	6	2	0	1	1	0	0	2	0	0	0	0	1	5	0	0	0
Intoxications	7	9	2	4	0	0	0	0	4	1	0	0	0	3	5	1	0	0
Septicemia.....	3	11	1	3	1	0	0	0	3	0	0	1	0	8	2	1	0	0
Dysentery	1	1	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
Typhoid fever.....	4	6	0	1	1	0	0	0	1	0	0	0	4	0	2	0	0	0
Other infections	5	5	1	0	1	0	0	0	2	0	0	0	0	3	1	1	0	0
Tuberculosis.....	3																	
Pneumonia	1																	
Balantidium coli	1																	
Diphtheria.....	1																	
Purpura hemorrhagica.....	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Benzol poisoning.....	0	0	0	0	0	0	0	0	0	0	0	0	5	0	2	1	0	0
Tumors (carcinomata).....	5	5	1	2	1	0	0	0	1	0	0	0	0	2	3	0	0	0

* Probable. †(Approx.)

All blood, before transfusion, was tested in the majority of cases by Dr. Guthrie or his assistants. He has kindly given me the following directions for these tests:

DIRECTIONS FOR TESTING DONORS FOR TRANSFUSION.

1. From 2 to 5 cubic centimeters of blood are withdrawn by venapuncture and allowed to clot in a Wassermann tube.
2. One drop of blood is dropped into a test-tube contain-

the development of iso-hemolysins. It is, therefore, most important that the bloods be matched before each transfusion.

BIBLIOGRAPHY.

1. Leviticus, XVII, 11.
2. Ovid's Metamorphoses, Book VII, 332 to 334.
3. Lowthrop, John: The Philosophical Transactions and Collections of Medical and Philological Papers, London, 1731.
4. Villari: Life of Savonarola.

5. Mathews, A. H.: Life and Times of Rodrigo Borgia, 1912. (Brentano.)
6. Birch: History of the Royal Society, Vol. II, pp. 123-125.
7. Halsted, William S.: Refusion in the Treatment of Carbonic Oxide Poisoning. *Ann. of Anat. & Surg.*, Jan., 1884.
8. Lindeman, Edward: Blood Transfusion by the Syringe and Cannula System. *J. Am. Med. Ass.*, 1914, LXIII, 1542. Blood Transfusion. Report of One Hundred and Thirty-five Transfusions by the Syringe-Cannula System. *J. Am. M. Ass.*, March 28, 1914, Vol. LXII, pp. 993-996. *Am. J. Obst.*, 1913, Vol. LVIII, p. 366; *Am. J. of Dis. of Children*, VI, 1913, p. 28.
9. Ziemssen (von): Ueber die Subcutane Blutinjection und über eine einfache Methode der intravenösen Transfusion. *Münch. Med. Wchnschr.*, 1892, Nr. 19, p. 323.
10. Carrel: Numerous publications.
11. Crile: Hemorrhage and Transfusion. (Appleton.) 1909.
12. Elsberg, Charles A.: A Simple Cannula for the Direct Transfusion of Blood. *J. Am. M. Ass.*, March 13, 1909.
13. Sauerbruch: *Münch. Med. Wchnschr.*, 1915, LXII, Nr. 45.
14. Hartwell, John A.: A Simple Method of Blood Transfusion with Cannula. *J. Am. M. Ass.*, Jan. 23, 1909.
15. Levin, Isaac: Plastic Surgery of Blood Vessels and Direct Transfusion of Blood. *New York, Ann. of Surg.*, May, 1913.
16. Janeway, Henry H.: An Improved Device for Transfusion. *Ann. Surg.*, 1911, LXIII, 720.
17. Soresi, A. L.: New Instrument for Direct Transfusion of Blood and Temporary Anastomosis Between Blood Vessels. XVI. International Medical Congress, Budapest, Aug.-Sept., 1909.
18. McGrath, Bernard Francis: A Simple Instrument for Transfusion. Rochester, Minn. *J. Am. Med. Ass.*, Jan. 3, 1914.
19. Libman, E., and Ottenberg, R.: A Practical Method for Determining the Amount of Blood Passing over during Direct Transfusion. *J. Am. M. Ass.*, March 7, 1914.
20. Landois, L.: Die Transfusion des Blutes. Berlin, 1866, Leipzig, 1875.
21. Brewer, George Emerson, and Leggett, Noel B.: Direct Blood Transfusion by Means of Paraffin-Coated Glass Tubes. *Surg. Gynec. & Obst.*, Sept., 1909.
22. Pope, Laxton: Simplified Transfusion. *J. Am. M. Ass.*, Apr. 26, 1913.
23. Bernheim, Bertram M.: *J. Am. M. Ass.*, 1912, Apr. 6, 1007.
24. Curtiss, A. H., and David, V. C.: Transfusion of Blood by a New Method, Allowing Accurate Measurement. *J. Am. M. Ass.*, Jan. 7, 1911, p. 35. Also: The Transfusion of Blood, Oct. 28, 1911, p. 1453.
25. Kimpton, A. R., and Brown, J. Howard: A New and Simple Method of Transfusion. *J. Am. M. Ass.*, July 12, 1913.

26. Satterlee and Hooper: The Further Development of an Apparatus for the Transfusion of Blood. *Surg. Gynec. & Obst.*, 1914, XIX, 235.
27. Percy, N. M.: A Simplified Method of Blood Transfusion with Report of Six Cases of Pernicious Anemia Treated by Massive Blood Transfusion and Splenectomy. *Surg. Gynec. & Obst.*, 1915, XXI, 360.
28. Blundell, James: Experiment on the Transfusion of Blood by the Syringe. *Med.-Chir. Tr.*, London, 1818, Vol. IX, 56-92.
29. Kush, Morris: An Automatic Transfusion Apparatus. *J. Am. M. Ass.*, Oct. 2, 1915.
30. Bernheim, Bertram M.: A Simple Instrument for the Indirect Transfusion of Blood. *J. Am. Ass.*, Oct. 9, 1915.
31. Cooley, Thomas B., and Vaughan, J. Walter: A Simple Method of Blood Transfusion. *J. Am. M. Ass.*, Feb. 8, 1913, p. 435.
32. Unger, Lester J.: A Method of Syringe Transfusion. *J. Am. M. Ass.*, Feb. 13, 1915. Recent Simplifications of the Syringe Method of Transfusion. *J. Am. M. Ass.*, Sept. 18, 1915, Vol. LXV.
33. Abel, John: Plasma Removal with Return of Corpuscles (Plasmapheresis). *J. Pharmacol. & Exp. Ther.*, 1913-14, V, 625.
34. Hustin. *Ann. et. Bull. Soc. méd. et nat.*, Bruxelles, 1914, No. 4, 104.
35. Weil, Richard J.: Sodium Citrate in the Transfusion of Blood. *J. Am. M. Ass.*, Jan. 30, 1915, p. 425.
36. Lewisohn: *Med. Rec.*, Jan. 23, 1915. *Surg. Gynec. & Obst.*, 1915, XXXI, No. 1.
37. Moss, W. L.: A Simple Method for the Indirect Transfusion of Blood. *Am. J. of the Med. Sciences*, May, 1914, No. V, Vol. CXLVII, p. 698.
38. Hayem. *De la transfusion du sang*, 1882.
39. Pool, Eugene H., and McClure, R. D.: Transfusion by Carrel's End-to-End Suture Method. With Report of Cases. *Ann. Surg.*, October, 1910.
40. McClure, Roy D.: Pernicious Anemia Treated by Splenectomy and Systematic Often-Repeated Transfusion of Blood. *J. Am. M. Ass.*, Sept. 9, 1916.

GENERAL REFERENCES.

- Ottenberg, R., and Libman, E.: Blood Transfusions; Indications; Results; General Management. *Am. J. Med. Sciences*, July, 1915, CL, p. 36.
- Oré, Pierre: *Études physiologiques sur la transfusion du sang*. Baillière et Fils, Paris, 1856.
- On the Operation of Transfusion—Being the Report of a Committee, by N. B. Benedict, M. D. *New Orleans Med. & Surg. Journ.*, July, 1853.

Case	Age	Sex	Diagnosis	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
T. A.	38	M.	Pernicious anemia. Pyorrhœa alveolaris. Splenectomy.	1st	Mar. 9, 1915	700	Lindeman	None
				2d	Mar. 26, 1915	750	Lindeman	None
				3d	July 3, 1915	650	Lindeman	None
				4th	July 10, 1915	675	Lindeman	None
				5th	July 24, 1915	700	Lindeman	None
				6th	Aug. —, 1915	700	Lindeman	None
				7th	Aug. 27, 1915	700	Lindeman	None
				8th	Sept. 1, 1915	625	Lindeman	None
				9th	Sept. 3, 1915	675	Lindeman	None
				10th	Sept. 9, 1915	675	Lindeman	None
				11th	Sept. 11, 1915	880	Lindeman	None
				12th	Sept. 23, 1915	770	Lindeman	None
				13th	Oct. 7, 1915	675	Lindeman	None
P. B.	42	M.	Pernicious anemia	1st	Jan. 23, 1915	650	Lindeman	Severe reaction. Chill. Temperature 105°. Pulse 120. No hemoglobinuria or jaundice.
J. B.	43	F.	Pernicious anemia. Pyorrhœa alveolaris. Splenectomy.	1st	Sept. 25, 1915	800	Lindeman	Slight temperature reaction. No chill. Urticaria and itching. No hemoglobinuria.
				2d	Sept. 30, 1915	900	Lindeman	None
				3d	Oct. 9, 1915	900	Lindeman	None
				4th	Oct. 16, 1915	900	Lindeman	None
				5th	Oct. 24, 1915	20	Lindeman	Marked. Temperature 102°. Chill and hemoglobinuria. Second test of blood showed hemolysis and agglutination.
				6th	Oct. 30, 1915	900	Lindeman	None
				7th	Dec. 11, 1915	788	Lindeman	None
				8th	Dec. 14, 1915	900	Lindeman	None
				9th	Dec. 18, 1915	800	Lindeman	None
				10th	Dec. 21, 1915	280	Lindeman	None
				11th	Dec. 30, 1915	550	Lindeman	Temperature rose to 101.5°. Chill. Urticaria. No hemoglobinuria. No jaundice.
H. P.	62	M.	Pernicious anemia. Splenectomy	12th	Jan. 22, 1916	500	Lindeman	None
				13th	Feb. 12, 1916	660	Lindeman	Temperature rose to 101.3°. No other reaction.
				14th	Feb. 14, 1916	270	Lindeman	None
				1st	Jan. 12, 1916	200	Unger apparatus.	Temperature rose to 103°. Violent chill. Collapse. No hemoglobinuria. No hemolysis or agglutination.
				2d	Jan. 21, 1916	300	Lindeman	None
				3d	Jan. 24, 1916	682	Lindeman	Temperature rose to 101°. No other reaction.
				4th	Jan. 26, 1916	640	Lindeman	Temperature 100°. No other reaction.
				5th	Feb. 2, 1916	630	Lindeman	Patient vomited. Two urticarial lesions. No temperature reaction. No hemoglobinuria. Felt chilly. No chill.
				6th	Feb. 7, 1916	660	Lindeman	Temperature rose to 101.6°. Felt chilly. No chill. No other reaction.
				7th	Feb. 19, 1916	450	Lindeman	Temperature rose to 102°. No other reaction.
M. C.	54	F.	Pernicious anemia	8th	Feb. 26, 1916	360	Lindeman	None
				9th	Mar. 6, 1916	500	Lindeman	Temperature rose to 101°. Many patches of urticaria. No hematuria. Slight shaking chill. Patient not uncomfortable.
				10th	Mar. 13, 1916	450	Lindeman	Temperature rose to 100°. No urticaria or hematuria.
N. D.	57	M.	Pernicious anemia. Hypertension	1st	Nov. 17, 1915	250	Lindeman	Slight rise in temperature. No other reaction.
				2d	Dec. 5, 1915	320	Lindeman	Temperature rose to 101.6°. No other reaction. No hemoglobinuria.
N. D.	57	M.	Pernicious anemia. Hypertension	1st	Oct. 21, 1915	662	Lindeman	Severe chill. Temperature rose to 105.7°. Hemoglobinuria for 2 hours. Hemolysis and agglutination. Jaundice.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
?	?	25	33	8	1,428,000	1,920,000	492,000	Incision for vein.....	Beneficial	1
?	?	54	67	13	2,128,000	2,440,000	312,000	Following this transfusion the patient was discharged from hospital.	Beneficial	2
?	?	29	40	11	840,000	1,656,000	816,000	Returned to hospital in poor condition (absent three months).	Beneficial	3
?	?	32	41	9	1,296,000	2,128,000	832,000	Beneficial	4
?	?	35	?	?	1,884,000	?	?	Splenectomy following transfusion.....	Beneficial	5
?	?	29	45	16	?	?	?	Beneficial	6
100	100	40	60	20	1,888,000	3,220,000	1,332,000	Interval of 11 days between blood counts.....	Beneficial	7
No change	?	50	60	10	1,960,000	3,088,000	1,128,000	Beneficial	8
?	?	60	70	10	3,088,000	3,144,000	56,000	Beneficial	9
?	132	60	65	5	2,424,000	?	?	Beneficial	10
?	130	65	75	10	2,424,000	3,688,000	1,264,000	Beneficial	11
?	130	80	85	5	3,632,000	4,432,000	800,000	Incision for vein.....	Beneficial	12
?	120	80	90	10	4,928,000	5,280,000	352,000	Jan. 17, 1916. Hb. 93%. Over three months without treatment.	Beneficial	13
?	?	25	39	14	960,000	1,680,000	720,000	No benefit	14
70	115/60	20	35	15	680,000	1,520,000	840,000	Beneficial	15
70	122/70	35	45	10	1,664,000	2,048,000	384,000	Beneficial	16
?	?	55	76	21	2,240,000	3,520,000	1,280,000	Following these transfusions patient says she feels "stuffed" and that the eyelids feel thick and swollen.	Beneficial	17
?	?	76	85	9	2,432,000	4,176,000	1,744,000	Beneficial	18
55	?	85	52	*33	4,176,000	2,672,000	*1,504,000	Marked decrease in R. B. C. and hemoglobin.....	Harmful	19
?	?	47	62	15	3,624,000	4,000,000	376,000	Patient discharged from hospital following this transfusion greatly improved.	Beneficial	20
?	?	22	40	18	648,000	2,158,000	1,510,000	Patient returned to hospital. Condition same as on first admission, poor. Absent 41 days.	Beneficial	21
?	?	42	55	13	2,450,000	3,158,000	708,000	Beneficial	22
30	170/100	?	?	?	?	?	?	Beneficial	23
100	?	?	48	?	?	3,000,000	?	Splenectomy Dec. 21, 1915. Transfusion 12 hours later.	Beneficial	24
72	142/85	53	48	5	1,900,000	?	?	No agglutination or hemolysis.....	No benefit	25
?	?	51	70	19	3,368,000	3,648,000	280,000	Two days between blood counts.....	Beneficial	26
?	?	74	78	4	3,792,000	?	?	Beneficial	27
?	?	78	82	4	?	?	?	Patient discharged	Beneficial	28
?	?	26	23	*3	1,224,000	1,440,000	216,000	Harmful	29
?	?	21	26	5	1,440,000	1,448,000	8,000	Beneficial	30
?	?	29	36	7	2,352,000	2,608,000	256,000	Beneficial	31
...	...	36	50	14	2,352,000	2,416,000	64,000	Beneficial	32
...	...	50	55	5	2,416,000	2,434,000	28,000	Beneficial	33
...	...	54	65	11	3,040,000	4,680,000	1,640,000	Feb. 12, 1916. Splenectomy.....	Beneficial	34
...	...	65	?	?	2,482,000	2,726,000	244,000	Beneficial	35
...	...	63	3,072,000	Beneficial	36
...	...	70	76	6	3,752,000	3,824,000	72,000	Beneficial	37
...	...	71	86	15	3,584,000	4,736,000	1,152,000	Beneficial	38
...	...	77	84	7	2,424,000	3,244,000	1,020,000	Spinal cord Ss. prominent.....	No benefit	39
...	...	77	?	?	3,472,000	?	?	Patient discharged	No benefit	40
160/75	31	35	4	4	1,280,000	1,208,000	*72,000	Three days later patient perfectly recovered. Hb. 30%. R. B. C. 1,208,000.	Harmful	41

Case.	Age.	Sex.	Diagnosis.	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
R. H.	M.	Pernicious anemia. Oral sepsis. Large spleen.	1st	June 22, 1915	610	Lindeman	Temperature rose to 105°. Brownish eruption on body. Hemorrhagic areas on arms. Marked hemoglobinuria.
F. I.	44	M.	Pernicious anemia	1st	Mar. 25, 1907	1280*	Suture of vein to artery.	None
T. M.	54	M.	Pernicious anemia	1st	Dec. 9, 1915	638	Lindeman	None
R. M.	27	M.	Pernicious anemia. Cord changes	1st	Oct. 29, 1914	540	Lindeman	None
				2d	Nov. 14, 1914	500	Lindeman	Temperature 101° for 24 hours following transfusion. 48 hours later rose to 105°. Edema of extremities. Râles in lungs. No hemoglobinuria.
L. O'F.	37	F.	Pernicious anemia	1st	May 24, 1915	660	Lindeman	None
E. W.	35	F.	Pernicious anemia. Splenectomy	1st	Feb. 3, 1914	?	Elsberg Cannula-Rachal artery to saphenous vein.	None
M. W.	55	F.	Pernicious anemia	1st	Oct. 23, 1915	750	Lindeman	Urticaria appeared 10 minutes after completion of transfusion. No other reaction.
S. H.	M.	Pernicious anemia. Splenectomy	1st	April 4, 1915	380	Lindeman	None
				2d	April 9, 1915	660	Lindeman	None
				3d	April 17, 1915	600	Lindeman	None
				4th	April 24, 1915	625	Lindeman	None
				5th	April 30, 1915	560	Lindeman	None
				6th	May 14, 1915	650	Lindeman	None
				7th	May 28, 1915	600	Lindeman	None
				8th	Aug. 22, 1915	..	Lindeman	None
				9th	Aug. 29, 1915	900	Lindeman	None
				10th	Sept. 11, 1915	726	Lindeman	None
				11th	Sept. 19, 1915	484	Lindeman	None
R. A.	45	M.	Chronic nephritis and myocardial insufficiency with secondary anemia.	1st	Feb. 26, 1915	550	Lindeman	None
H. A.	M.	Papilloma of bladder. Secondary anemia.	1st	Aug. 23, 1912	?	Direct transfusion. Artery to vein.	Temperature 101° following transfusion. No other reaction. Blood in urine continuously before transfusion.
N. B.	11	M.	Burns on legs. Secondary anemia	1st	Sept. 7, 1915	484	Lindeman	Temperature rose to 103°. No other reaction.
R. B.	1½ mo.	F.	Secondary anemia. Syphilis. Pneumonia. Otitis media.	1st	Nov. 18, 1915	110	Lindeman	Temperature rose to 101°. No other reaction.
I. B.	26	F.	Submucous sarcoma (uterus). Secondary anemia.	1st	Oct. 15, 1915	200	Lindeman	Vomited. Air hunger. Death. Patient was practically moribund prior to transfusion and operation. Tests showed no agglutination, hemolysis (?).
R. C.	20	F.	Chronic pelvic inflammatory disease. Secondary anemia.	1st	Feb. 12, 1915	300	Lindeman	Severe reaction. Vomiting. Collapse. Temperature 103.4°. Pulse 170. Chill.
H. C.	1	F.	Foreign body in intestine. Secondary anemia.	1st	Sept. 6, 1915	250	Lindeman	Temperature rose to 104°. No other reaction.
R. C.	2 mos.	F.	Secondary anemia	1st	Oct. 9, 1915	110	Lindeman	Temperature rose to 102°. No other reaction.
				2d	Oct. 30, 1915	115	Lindeman
				3d	Jan. 21, 1916	100	Lindeman
				4th	Feb. 24, 1915	160	Lindeman
V. C.	26	M.	Brain tumor, cerebral, left. Secondary anemia.	1st	Nov. 4, 1914	600	Lindeman	None
W. D.	2 mos.	M.	Alimentary intoxication. Secondary anemia.	1st	July 27, 1915	30	Lindeman	None
N. H.	2	M.	Third degree burns, legs and body. Secondary anemia.	1st	Dec. 31, 1915	130	Lindeman	Temperature became subnormal. Child seemed worse.
O. H.	Baby	M.	Alimentary intoxication. Secondary anemia.	1st	Aug. 7, 1915	100	Lindeman	None
C. M.	9	M.	Splenomegaly. Secondary anemia	1st	May 10, 1912	?	Direct transfus'n. Radial artery to basilic vein.	None
A. P.	5	F.	Burns, abdomen and thighs. No anemia.	1st	Nov. 3, 1910	?	Direct transfus'n. Radial artery to vein.	None
H. R.	26	F.	Gastric ulcer. Chronic nephritis. Arteriosclerosis. Secondary anemia.	1st	Jan. 10, 1915	850	Lindeman	Vomited. Hemoglobinuria. Death.
R. S.	3	M.	Mongolian idiocy. Secondary anemia.	1st	Oct. 30, 1915	274	Lindeman	Temperature rose to 103.2°.
J. S.	22	M.	Congenital syphilis. Ulcer of legs. Secondary anemia.	1st	April 19, 1915	625	Lindeman	None
R. S.	2½	M.	Duodenal ulcer. Intestinal indigestion. Secondary anemia.	1st	Sept. 21, 1915	133	Lindeman	None

* Estimated.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
?	?	34	35	1	1,430,000	?	?	During transfusion patient complained of nausea and pain in back.	Harmful	42
?	?	22	38	16	848,000	1,880,000	1,032,000	16 c. c. of blood collected from Radial in one minute at close of transfusion. Amount roughly estimated.	Beneficial	43
4/60	108/63	57	62	5	1,126,000	3,000,000	1,874,000	Beneficial	44
?	?	21	34	7	1,024,000	1,584,000	560,000	No benefit	45
?	?	35	39	4	1,504,000	1,800,000	296,000	Very atypical reaction.....	Harmful	46
?	?	44	56	12	1,672,000	2,272,000	400,000	Patient discharged	Beneficial	47
?	?	35	56	21	1,504,000	2,228,000	1,724,000	Splenectomy performed with transtusion in progress.	Beneficial	49
5/70	130/90	32	50	18	1,528,000	2,864,000	1,336,000	Beneficial	50
?	?	22	27	5	1,200,000	?	?	Beneficial	51
?	?	29	39	10	1,180,000	1,832,000	652,000	Beneficial	52
?	?	37	43	6	2,016,000	2,408,000	392,000	Beneficial	53
?	?	41	47	6	2,252,000	2,660,000	408,000	Beneficial	54
?	?	46	55	9	2,552,000	2,960,000	408,000	Beneficial	55
?	?	48	58	10	2,370,000	2,992,000	622,000	Splenectomy May 18, 1915.....	Beneficial	56
?	?	34	50	16	2,168,000	?	?	Lues	Beneficial	57
100	100	14	32	18	960,000	1,352,000	392,000	Beneficial	58
124	124	33	46	13	1,352,000	?	?	Beneficial	59
98	115	32	42	10	1,400,000	2,392,000	992,000	Beneficial	60
105	112	33	42	9	1,480,000	1,880,000	400,000	Beneficial	61
?	?	60	65	5	3,104,000	4,024,000	80,000	400 c. c. withdrawn from patient. 550 c. c. of blood from daughter injected.	Beneficial	62
?	?	18	39	21	?	?	?	Beneficial	63
?	?	39	61	21	?	3,860,000	?	Beneficial	64
?	?	14	38	24	?	2,712,000	?	Blood injected into external jugular vein.....	Beneficial	65
?	?	15	?	?	?	?	?	Uterus curetted and packed.....	Harmful	66
?	?	20	24	4	1,200,000	?	?	5 c. c. of vital red intravenously by Dr. Rowntree.....	Harmful	67
?	?	40	52	12	2,442,000	?	?	Beneficial	68
?	?	15	58	43	?	?	?	Incision for vein at elbow.....	Beneficial	69
?	?	Blood injected into longitudinal sinus.....	Beneficial	70
?	?	Incision for vein.....	Beneficial	71
?	?	14	Given into vein on back of hand. Incision for vein...	Beneficial	72
115	?	45	55	10	2,680,000	3,800,000	1,120,000	Two operations prior to transfusion with much hemorrhage.	Beneficial	73
...	?	?	?	Injected into longitudinal sinus.....	No benefit	74
?	?	34	35	1	?	?	?	Injected into longitudinal sinus.....	Harmful	75
...	No benefit	76
...	...	10	23	13	?	1,885,000	?	Beneficial	77
?	?	90	93	3	4,600,000	4,500,000	100,000	Probably no blood given.....	No benefit	78
8/100	200/135	25	43	18	3,230,000	?	?	Patient vomiting blood prior to transfusion. Autopsy.	Harmful	79
?	?	18	55	37	768,000	2,768,000	2,000,000	Incision for vein.....	Beneficial	80
?	?	36	48	12	1,680,000	2,464,000	784,000	Beneficial	81
?	?	40	40	0	?	?	?	Incision for vein.....	No benefit	82

Case.	Age.	Sex.	Diagnosis.	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
G. T.	6 mos.	F.	Acute intestinal indigestion. Secondary anemia.	1st	July 27, 1915	45	Lindeman	Severe. Temperature rose to 103.5° same night. To 105° next night and to 105° next. Death. No jaundice. No urinalysis.
B. T.	2 wks.	F.	Bleeding from umbilical cord stump. Secondary anemia. Syphilis (?).	1st	July 10, 1915	50	Lindeman	None
M. T.	54 yrs.	M.	Gallstone in common duct operation. Secondary anemia.	1st	April 3, 1915	520	Lindeman	Chill. Temperature rose to 103.8° No hemoglobinuria.
H. M.	1½	M.	Hemophilia. Secondary anemia.	1st	June 8, 1915	100	Lindeman	None
				2d	Aug. 6, 1915	100	Lindeman	None
				3d	Aug. 10, 1915	254	Lindeman	None
				4th	Aug. 14, 1915	275	Lindeman	None
C. S.	24	M.	Hemophilia. Chronic arthritis..	1st	Sept. 4, 1915	66	Lindeman	None
E. H.	39	M.	Brain tumor. Operation. Hemorrhage. Shock.	1st	Sept. 9, 1915	300	Lindeman	None as far as could be observed.
F. H.	16	M.	Rupture of kidney. Hemorrhage. Shock.	1st	Jan. 10, 1912	?	Direct transfus'n. Crile clamp.	None
W. S.	19	M.	Typhoid fever. Second perforation. Hemorrhage. Shock.	1st	Dec. 31, 1915	400	Lindeman	None
A. S.	25	F.	Colloid goitre. Hyperthyroidism. Operation. Hemorrhage. Shock	1st	Nov. 14, 1915	420	Lindeman	None
T. C.	37	M.	Duodenal ulcer. Acute alcoholic gastritis. Hemorrhage.	1st	Feb. 5, 1915	500	Lindeman	None
E. B.	2	F.	Leukemia	1st	Oct. 5, 1915	120	Lindeman	None immediately. Transfusion done at another hospital.
J. S.	31	M.	Acute myeloid leukemia. Bronchopneumonia. Adherent pericardium.	1st	Dec. 19, 1909	?	Crile-Bernheim Cannula. Artery to vein.	None
				2d	Jan. 2, 1910	?	Direct method. Crile Cannula. Artery to vein.	None
C. S.	7	M.	Acute leukemia	1st	May 16, 1913	?	Direct	Temperature rose to 103°. Rales in lungs. Cough. Dyspnoea.
G. W.	25	F.	Chronic myeloid leukemia. Hemorrhagic diathesis.	1st	Nov. 30, 1915	520	Lindeman	Temperature rose slightly. Chill. No hemoglobinuria. No other reaction.
E. S.	26	M.	Splenomyelogenous leukemia. Epistaxis. Secondary anemia.	1st	July 7, 1913	?	Direct transfus'n. Esmarch Cannula. Artery to vein.	None. Patient moribund when taken to operating room and died on table.
J. B.	1	M.	Intestinal indigestion. Acidosis.	1st	Feb. 5, 1916	155	Lindeman	Temperature rose to 102.5°.
B. B.	32	F.	Chronic nephritis. Myocardial insufficiency. Secondary anemia. Uræmia.	1st	Nov. 11, 1914	600	Lindeman	Temperature 100°. Body and limbs itched for 24 hours. Some nausea. No hemoglobinuria.
				2d	Dec. 8, 1914	400	Lindeman	Temperature rose to 104.4°. Blood pressure fell 100 mm. Hg. Several convulsions.
				3d	Dec. 12, 1914	500	Lindeman	None
P. K.	21	M.	Chronic nephritis. Secondary anemia. Uræmia. Myocardial insufficiency.	1st	Jan. 22, 1916	600	Lindeman	Temperature rose to 102.5°.
M. P.	3 wks.	F.	Acute intestinal indigestion. Acidosis.	1st	Jan. 8, 1916	22	Lindeman	None
E. W.	34	M.	Chronic nephritis. Uræmia. Secondary anemia. Oedema lungs.	1st	April 21, 1915	500	Lindeman	Patient died a few hours later of pulmonary oedema.
J. M.	28	M.	Pyelonephritis. Cystitis. Septicæmia.	1st	Dec. 2, 1914	240	Lindeman	Became restless, nervous, cyanotic dyspnoic and died on table. Hemolysis.
G. R.	27	M.	Gonococcus septicæmia. Acute nephritis. Endocarditis.	1st	Oct. 24, 1914	325	Lindeman	None
				2d	Oct. 31, 1914	600	Lindeman	None
C. S.	45	M.	Streptococcus septicæmia	1st	Nov. 24, 1915	205	Lindeman	None
				2d	Dec. 11, 1915	220	Lindeman	None
				3d	Dec. 20, 1915	250	Lindeman	None
				4th	Jan. 7, 1916	200	Lindeman	Temperature rose 1°.
				5th	Jan. 26, 1916	176	Lindeman	Temperature reached 103°, but usual evening rise for this patient was to 102-103°.
D. W.	20	F.	Bacillary dysentery (Shigo). Pulmonary tuberculosis.	6th	Feb. 10, 1916	257	Lindeman	None apparently.
				1st	Oct. 30, 1915	800	Lindeman	Difficult to judge. Patient markedly jaundiced next day. Moribund when transfusion was done.
R. B.	24	M.	Typhoid fever. Relapse. Hemorrhage. Otitis media. Cervical adenitis. Parotitis.	1st	May 21, 1915	600	Lindeman	Wonderful improvement. Temperature fell from 103° to 100.5°. Pulse from 140 to 108. Blood pressure rose 18 mm. Hg. Bleeding from intestine ceased.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
...	Incision for vein—leg.....	Harmful	83
?	?	30	50	20	Beneficial	84
?	?	?	64	?	?	?	?	Patient bled slowly but steadily after operation. Transfusion caused no cessation.	No benefit	85
...	...	22	37	15	2,472,000	2,854,000	382,000	Patient bleeding from wound on tongue; ceased following transfusion.	Life saving	86
...	...	?	35	?	?	?	?	Again bleeding. Ceased with transfusion.....	Life saving	87
...	...	28	55	27	?	?	?	Again bleeding. Suture of wound ineffectual several times.	Life saving	88
...	...	55	92	37	?	?	?	Wound healing	Life saving	89
?	?	80	?	?	?	?	?	No benefit	90
?	?	?	?	?	?	?	?	Patient moribund. Blood not tested for agglutination or hemolysis. Perhaps slight temporary benefit. Patient died in 18 hours.	No benefit	91
...	...	?	62	?	?	3,920,000	?	Beneficial	92
...	Patient died a few hours after transfusion and second perforation and operation.	No benefit	93
?	?	?	68	?	?	2,624,000	?	Beneficial	94
13/64	?	54	?	?	3,350,000	?	?	Patient vomited large amounts of blood. Operation. Ligature of bleeding vessel. Death two hours later.	No benefit	95
84	108	?	?	?	?	?	?	Patient died a few weeks later.....	No benefit	96
?	?	20	25	5	840,000	1,130,000	290,000	Patient bled from incision made for vein.....	No benefit	97
?	?	20	31	11	960,000	1,224,000	264,000	Patient oozed from incision made for veins. Hb. soon fell to former level.	No benefit	98
?	?	27	43	16	1,990,000	2,400,000	410,000	Patient died six weeks later.....	No benefit	99
?	?	30	37	7	2,432,000	2,756,000	324,000	Wound on back from which patient had oozed at intervals for 20 days and had not healed, ceased oozing and healed rapidly.	Beneficial	100
?	?	10	?	?	1,092,000	No benefit	101
...	60 c. c. of blood withdrawn and 155 c. c. injected.....	No benefit	102
...	...	38	52	14	2,984,000	3,996,000	112,000	Beneficial	103
...	...	46	45	*1	2,920,000	2,376,000	*544,000	Plasmaphæresis	Harmful	104
160	190	41	47	6	?	?	?	500 c. c. first withdrawn from patient, then 500 c. c. of husband's blood injected.	Beneficial	105
...	...	26	37	11	2,088,000	2,200,000	112,000	General condition improved.....	Beneficial	106
...	...	32	?	?	1,500,000	?	?	Injected into longitudinal sinus. Small cephalohæmatoma.	No benefit	107
...	Harmful	108
...	...	19	?	?	1,712,000	Harmful	109
00	108	22	26	4	?	?	?	Beneficial	110
1/65	118/80	23	30	7	1,650,000	2,150,000	500,000	No influence on septicæmia. Incision for vein.....	Beneficial	111
06	124	77	?	?	3,976,000	?	?	No benefit	112
/65	94/75	77	78	1	3,328,000	?	?	Donor vaccinated with streptococcus causing septicæmia in recipient.	No benefit	113
1/90	128/95	?	78	?	?	?	?	Same donor	No benefit	114
?	?	?	?	?	?	?	?	Same donor	No benefit	115
?	?	?	75	?	?	4,368,000	?	Blood cultures from patient showed no decrease in number of organisms.	No benefit	116
?	?	?	?	?	?	?	?	117
?	?	65	?	?	5,672,000	?	?	Patient died 12 hours after transfusion.....	No benefit	118
/40	98/60	45	51	6	?	?	?	Patient practically moribund prior to transfusion....	Life saving	119

Case.	Age.	Sex.	Diagnosis.	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
R. B. —cont.	24	M.	Typhoid fever. Relapse. Hæmorrhage. Otitis media. Cervical adenitis. Parotitis.	2d	May 25, 1915	700	Lindeman	Chill. Rise in temperature. Gre improvement following. Temper ture normal next day.
S. D.	27	M.	Typhoid fever. Perforation. Sec- ondary anemia.	1st	Oct. 2, 1915	350	Lindeman	Temperature fell to normal 12 hou following transfusion. Then slow rose to former level 102-103°.
E. S.	25	M.	Typhoid fever. Hæmorrhage. Secondary anemia.	1st	Nov. 13, 1915	460	Lindeman	Pulse fell from 120 to 104. Stoppe bleeding from intestine. Temper ture fell. Patient greatly im proved.
				2d	Nov. 25, 1915	600	Lindeman	Pulse fell from 120 to 104 durin transfusion. Temperature fro 104.2° to 100° in next 12 hour Stopped bleeding.
G. H.	7 wks.	F.	Diphtheria. Primary anemia...	1st	Nov. 4, 1914	60	Lindeman	Temperature rose to 103°. No oth reaction. Temperature elevatio commenced prior to transfusio Probably no association.
E. K.	5	M.	Tuberculous enteritis. Secondary anemia.	1st	Dec. 29, 1915	350	Lindeman	None
C. L.	7	M.	Tuberculous splenomegaly	1st	May 14, 1914	?	Direct transfus'n.	None
H. W.	25	M.	Balantidium coli infection. Myo- cardial insufficiency. Second- ary anemia.	1st	May 12, 1915	375	Lindeman	Temperature rose to 105°. Pulse 14 Collapse. No hemoglobinuria.
J. G.	44	F.	Purpura hæmorrhagica	1st	Aug. 31, 1915	330	Lindeman	None
F. C.	14	F.	Benzol poisoning	1st	July 8, 1909	?	Direct. Crile Clamp.	None
				2d	July 12, 1909	?	Direct. Crile Clamp.	None
S. H.	31	F.	Benzol poisoning	1st	May 3, 1914	?	Direct	None
				2d	May 17, 1914	?	Direct. Moss method.	Slight hemoglobinuria. No oth reaction.
				3d	May 23, 1914	?	Direct	None
				4th	May 31, 1914	?	Direct	None
				5th	June 13, 1914	?	Direct	None
M. W.	14	F.	Benzol poisoning	1st	July 3, 1909	?	Direct	None
J. F.	53	F.	Carcinoma stomach. Metastasis. Thrombus of superficial veins. Secondary anemia. Cerebral embolus.	1st	Nov. 8, 1915	788	Lindeman	Violent chill, elevation of temper ture. Pulse rose from 120 to 140.
J. J.	?	M.	Carcinoma prostate. Hæmor- rhage. Secondary anemia.	1st	May 28, 1915	?	Lindeman	None
D. J.	60	M.	Carcinoma stomach. Secondary anemia.	1st	Dec. 9, 1913	?	Direct transfus'n. Crile Cannula.	None
P. M.	40	M.	Carcinoma stomach. Abscess liver. Secondary anemia.	1st	July 3, 1915	600	Lindeman	Mild. Slight rise in temperatur No other reaction.
A. W.	F.	Carcinoma stomach. Metastasis. Secondary anemia.	1st	Sept. 9, 1915	484	Lindeman	Collapse. No temperature reactio Soon rallied. No cardiac dilat tion. No hemoglobinuria or jau dice.
H. P.	62	M.	Pernicious anemia (see this table, Reference Nos. 29-38).	11th	April 5, 1916	450	Lindeman	None
C. S.	45	M.	Streptococcus septicemia (see 112-117).	7th	Mar. 14, 1915	210	Lindeman	Temperature rose to 102.6°. Chil sensation but no shaking. N hematuria.
				8th	April 1, 1916	220	Lindeman	Temperature rose to 108°. No chil No hematuria.
				9th	May 1, 1916	264	Lindeman	No reaction.
T. D.	Baby.	F.	Bleeding from puncture wound on back.	1st	April 25, 1916	60	Lindeman	Temperature rose to 104°. Patien died nine hours afterward. N evidence of hypertransfusion.
J. W.	Baby.	M.	Acidosis following operation. Re- moval of omental cyst.	1st	April 21, 1916	47	Lindeman	Probably. No reaction from tran fusion. Child died 10 hours late
W. T.	54	M.	Pernicious anemia	1st	April 19, 1916	400	Lindeman	Temperature rose to 101.5°. Chi Urobilin + guaiac 0 (urine).
C. M.	47	F.	Pernicious anemia	1st	April 18, 1916	330	Lindeman	Patient's temperature became su normal then rose to 99.5°. Uroli lin +, guaiac negative (urine Patient died nine hours aft transfusion.
D. B.	55	M.	Pernicious anemia. Combined sclerosis. Splenectomy.	1st	April 8, 1916	440	Lindeman	None
E. C.	28?	F.	Typhoid fever. Pneumonia.....	1st	Mar. 30, 1916	496	Lindeman	Patient complained of pain in ba after transfusion. Died nine hou later. Moribund when transfuse
B. A.	Baby.	..	Bleeding from umbilical cord....	1st	Mar. 24, 1916	50	Lindeman	None
R. C.	F.	Primary anemia (see Nos. 69-72)	5th	Mar. 21, 1916	140	Lindeman	None
J. N.	Baby.	..	Malnutrition. Intoxication	1st	Mar. 14, 1916	130	Lindeman	Died five hours after transfusio No evidence of hypertransfusio

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
72	?	38	46	8	?	?	?	Donor had had typhoid fever. Great improvement....	Life saving	120
70	?	40	48	8	?	?	?	Patient died two hours later. Autopsy.....	Beneficial	121
...	...	28	Life saving	122
...	...	26	32	6	?	2,104,000	?	Incision for veins.....	Life saving	123
...	...	20	28	8	?	?	?	Injected into jugular vein (incision).....	Beneficial	124
?	?	?	36	?	?	2,400,000	?	24 hours later Hb. was 54%.....	Beneficial	125
?	?	35	60	25	?	?	?	Splenectomy later. Uneventful convalescence.....	Beneficial	126
?	?	16	20	4	?	?	?	Incision for vein.....	Harmful	127
?	?	75	?	?	4,064,000	?	?	No benefit. Patient died soon after leaving hospital of cerebral hemorrhage.	No benefit	128
?	?	28	28	0	2,128,000	2,160,000	*32,000	Transfusion not successful.....	Harmful	129
?	?	15	?	?	1,150,000	?	?	Transfusion not successful. Patient died short time later. Autopsy.	Harmful	130
?	?	20	38	18	1,226,000	1,680,000	454,000	Patient greatly improved. Bleeding ceased temporarily.	Life saving	131
?	?	28	48	20	1,117,000	1,971,000	864,000	May 14, 1914. 500 c.c. of defibrinated blood by Dr. Moss' method.	Life saving	132
?	?	20	40	20	910,000	1,856,000	946,000	Patient bleeding from m. m. except immediately after transfusions.	Life saving	133
?	?	24	42	18	?	?	?	Donor not tested for agglutination or hemolysis.....	Life saving	134
?	?	48	65	17	3,476,000	4,528,000	1,052,000	Patient has practically ceased bleeding. Regenerating. Perfect recovery.	Life saving	135
?	?	11	8	*3	544,000	640,000	96,000	Transfusion unsuccessful	Harmful	136
56	100/58	25	30	5	2,800,000	?	?	No benefit	137
?	?	15	30	15	?	2,160,000	?	Beneficial	138
?	?	34	50	16	?	?	?	Gastro-enterostomy and partial resection while transfusion was done.	Beneficial	139
?	?	30	42	12	2,592,000	3,553,000	961,000	Beneficial	140
?	?	?	?	?	?	?	?	No benefit	141
...	...	82	88	6	3,272,000	3,640,000	68,000	Second transfusion from this donor.....	Beneficial	142
?	?	?	67	?	?	?	?	Temperature rises less every P. M. than upon admission.	Beneficial (?) ...	143
?	?	73	?	?	?	?	?	Patient's condition improving.....	Beneficial (?) ...	144
?	?	57	70	13	?	?	?	Blood cultures in Nov., 1915, showed 50 colonies to c. c. April 21, 1916, 2 colonies.	Beneficial (?) ...	145
?	?	?	?	?	?	?	?	Reaction strongly suggested an agglutination and hemolysis.	Harmful	146
...	Moribund when transfused.....	No benefit	147
...	...	47	57	10	1,648,000	?	?	Beneficial	148
?	?	20	29	9	960,000	?	?	Patient moribund and with air hunger when transfused.	Harmful	149
?	?	85	100	15	3,048,000	3,952,000	904,000	Splenectomy on March 1, 1916.....	Beneficial	150
?	?	?	?	?	?	?	?	Transfusion done at home of patient.....	Questionable	151
?	?	?	?	?	?	?	?	Bleeding ceased. All other methods ineffectual.....	Beneficial	152
?	?	Beneficial	153
?	?	?	?	?	?	?	?	No benefit	† 154

Lost.

† In final balance one case must be subtracted (48 is vacant) making a total of 153 transfusions.

ALEUCOCYTHÆMIC LEUKÆMIA.

1. ACUTE MYELOBLASTIC LEUKÆMIA. 2. CHLOROMA (?). 3. CHRONIC LYMPHATIC LEUKÆMIA.

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In 1845 Hughes Bennett reported a case of a disease which he later called "leucocythæmia," or "white cell blood." Shortly after Bennett's publication, Virchow described a condition to which he gave the name "leukæmia," or "white blood."¹ The diseases recorded by these two observers were undoubtedly identical in nature, but "leukæmia" has gained general recognition as the name of this disease entity. In its etiological sense, however, neither term is always descriptive of the disease. There are instances of true leukæmia (as the name is now used) in which there is no increase of leucocytes in the circulating blood; hence "leukæmia" has come to be used as the name of the disease as a pathological condition, regardless of the leucocyte count. In describing cases of true leukæmia without leucocytosis of the blood, the term "aleukæmic leukæmia" is frequently used, or the expression "leukæmia in the aleukæmic state," or "stage." "Aleukæmic" here is used in its etiological sense, indicating an absence of leucocytosis of the blood, whereas "leukæmia" is used in its derived sense, to indicate the fundamental pathology of the disease. To use two words of the same origin together and give them entirely different meanings creates a paradox that is often confusing. The confusion is increased by the fact that the word "aleukæmic" is used not only to describe conditions in which there is no leucocytosis, but also conditions which are "aleukæmic" because they bear no relation to leukæmia.

Waterhouse² has reported cases of true leukæmia with qualitative blood changes but which showed no increase in the total number of white blood cells. "Aleucoeythæmic Leukæmia" is the title of his communication. This expression is not confusing, for the word "leucocythæmia" has retained its original significance, indicating an increase of white blood cells in the blood; moreover, it has its source in the original report of Bennett.

It is now well known that the number of leucocytes in the blood in true leukæmia may be normal or even subnormal. One or more of a variety of circumstances may be responsible for this condition. As the result of treatment with X-rays, arsenic, benzol, etc., the leucocytes not infrequently drop to a normal total count. Indeed, care must be taken in using these therapeutic agents to avoid too great a suppression of the leucocytes. Intercurrent infections, such as influenza, typhoid fever, tuberculosis and septicæmia, may cause a reduction of the leucocytes in leukæmia. There are certain cases of leukæmia in which the leucocyte count may be normal during some stage

of the disease, and others in which there probably never is a leucocytosis. Incipient cases are most apt to present a normal white cell count, but the same may occur in the terminal stage or during the course of the disease.

In most of the above cases a differential count would be expected to show an abnormal blood picture, usually with definitely immature cells. In such cases there is no doubt about the diagnosis of leukæmia. There is, however, a small group of cases to which the name "pseudoleukæmia" has been given by certain German writers. In these cases, the pathology is that of leukæmia, except that the blood picture is normal. In many instances, this condition passes into one of undoubted leukæmia, with characteristic blood changes. The attempt to create a separate disease entity of such cases of pseudoleukæmia has not met with general acceptance, as the difference between these conditions and leukæmia is slight.³

The Pappenheim school points out the advisability of sharply differentiating cases of aleukæmic (aleucoeythæmic) disease of the leucoblastic tissues from infectious granulomatous disease of this system and from lymphosarcoma and true tumors. They say, however, that the real hyperplastic pseudoleukæmia is only a particular form of chronic lymphadenoid leukæmia, and that the so-called medullary aleukæmic pseudoleukæmia shows the same diffuse changes in the bone-marrow as does the outspoken lymphadenoid leukæmia. Naegeli⁴ holds the same conception, and considers that aleukæmic lymphadenosis and myelosis (pseudoleukæmia or aleukæmia) should fall into the group of leukæmias. In brief, it may be said that the conditions classified by various authors as true pseudoleukæmia, either lymphatic or medullary, as aleukæmia, as aleukæmic lymphadenosis or myelosis, and as aleukæmic leukæmia, are probably all to be considered leukæmia at an aleucoeythæmic stage.

Other cases which can be differentiated by the history only from the group just described are those of leukæmia in remission. It is said that, in certain cases, remissions occur during which the blood picture may become perfectly normal. In some cases, the blood, spleen and all other tissues, so far as can be determined, may become perfectly normal during a remission.⁵

Chloroma is now generally recognized as a type of leukæmia characterized by green nodules, which have a predilection for the periosteum of certain bones. Cases of chloromatous leukæmia, according to Naegeli, are more apt to present "anæmic, aleukæmic and sublymphæmic" blood pictures than are other forms of leukæmia. Naegeli explains this fact by the

¹ Osler, Sir Wm.: The Principles and Practice of Medicine, 1912.

² Waterhouse, R.: Bristol Med. and Chir. Jour., 1913, XXXI, 10.

I wish to acknowledge with thanks the work of Mr. Martin of the Phipps Psychiatric Clinic in making photomicrographs of the blood.

³ Pappenheim, Baumgarten and others. Folia Hæmat., 1906, 453.

⁴ Naegeli, O.: Leukämie u. Pseudoleukämie, 1913.

⁵ Cabot, R. C.: Modern Medicine, Osler and McCrae, 1915.

hypothesis that the abnormal swelling of the chloroma tissue cells may prevent these cells from following the normal channels of passage into the blood stream. Only two cases are recorded, however, in which the aleucocythæmic condition of the blood persisted throughout the course of the disease. One is that of Bramwell,⁶ which ran a febrile course, with a lethal ending one month after the patient came under observation. The white cell count was never increased, although 95% or more were lymphocytes, chiefly large lymphocytes. Türk⁷ reported the other instance: this was a rapidly fatal case of chloroma, with a W. B. C. count between 2000 and 4100 per c. mm. There was a large lymphocyte percentage. The diagnosis was confirmed at autopsy.

In the records of The Johns Hopkins Hospital are 105 cases of leukæmia, of which 41 belong to the lymphatic, 64 to the myeloid variety. Five of the lymphatic leukæmia group were aleucocythæmic at some time. In one case the W. B. C. count fell from 33,500 to 1900 as a result of treatment with Fowler's solution, and the differential count became almost normal. Another case had a febrile course very similar to that of typhoid, during which the W. B. C. rose from 4300 to 16,800 (77.75% monos.). At discharge the blood presented a picture of chronic leukæmia—W. B. C. 5880, monos. 60.66%. A third case showed a fall of W. B. C. from 17,000 (large monos. 76.5%) to 6880 (64.5% monos.) following X-ray treatment and Fowler's solution. Another was a case of chronic aleucocythæmic lymphatic leukæmia or lymphadenosis, with a leucocyte count from 7200 to 9360, and the lymphocytes as high as 88.5%. Of the myeloid leukæmia cases, nine were aleucocythæmic at some stage. One acute case showed a normal total white cell count for a few weeks, while there were 73% myeloblasts. A few weeks before death there was, however, a flooding of the blood with white cells. Eight chronic myeloid cases were aleucocythæmic at some stage, five as the result of treatment, three spontaneously. No cases of chloroma are recorded.

During the past year three cases of leukæmia of the aleucocythæmic variety were studied at this hospital. In one of them an acute myeloblastic leukæmia, so far as is known, there was never a real leucocytosis; in the second, a case of chloroma, there was a history of a leucocytosis, but none was found in counts made several months apart; and in the third case, one of chronic aleucocythæmic lymphatic leukæmia, there was no leucocytosis prior to the terminal stage.

CASE.—Acute myeloblastic leukæmia. White school-girl, æt. 14.

Complaint.—Weakness.

Family History.—Negative, except for paresis in the father.

Past History.—Healthy girl. Two light attacks of scarlet fever, in infancy and at six years. Measles twice, at 10 and 12 years of age.

Present Illness.—The onset was three months before admission, with stiffness in the knees and pain on walking. Salicylates were ineffectual. No other joints were involved, but the pain in the knees continued until one month before admission. There was

progressive pallor and weakness. One small hemorrhagic spot was seen on the left arm. There was no œdema nor dyspnœa. She lost 15 pounds in weight. Both the patient and her mother noticed some fullness of the abdomen. One week before admission a consulting physician found the W. B. C. count 8000.

Examination on Admission.—The skin and mucous membranes were very pale. Nothing unusual was noticed as to the gums and tonsils. There were enlarged glands at the angles of the jaws, and firm, palpable posterior cervical glands; these glands were only moderately enlarged. The axillary glands were palpable, but neither large nor soft, and the inguinals were not felt. There was some retromanubrial dullness. The spleen was notched and reached to a level two finger-breadths above the left anterior superior spine, and just beyond the umbilicus on the right. The liver edge was just below the costal margin. There was a small cutaneous hemorrhage on the left arm, and hemorrhages in both retinae. An ankle clonus was obtained on the right side.

The Blood.—Bleeding time was definitely prolonged. Resistance of R. B. C. to hypotonic salt solutions was normal. There was marked anisocytosis and poikilocytosis of the red cells. R. B. C. 1,552,000. Hb. 25%. W. B. C. 7120.

Differential count (250 cells), Wilson stain:

Poly. Neut.	22.4	per cent.
Poly. Eosin.	0.4	"
Poly. Baso.	0.4	"
Large Mono.	0.4	"
Small Lymphocytes	0.4	"
Large Lymphocytes	1.2	"
Transitionals	0.0	"
Myeloblasts	57.6	"
Promyelocytes	1.6	"
Myelocytes (Neut.)	1.6	"
Myelocytes (Eosin.)	0.0	"
Myelocytes (Baso.)	0.4	"
Normoblasts	3.2	"
Intermediates	1.6	"
Megaloblasts	1.2	"
Smudges	6.4	"
Unclassified	1.2	"

100.0 per cent.

The predominating cell was a typical, large myeloblast. The protoplasm was not granular, stained rather deeply basophilic, and was frequently vacuolated. The protoplasm was often extremely scanty. It was sometimes even darker than the nucleus. The nuclei were usually round oval, often with an incisure; they stained less deeply than the average lymphocyte nuclei, and showed a very delicate reticulation.

The Wassermann reaction was negative. The urine was negative: it showed no Bence-Jones proteinuria. The temperature varied from 99.5° to 100.6° F.

The patient left the hospital after two days' observation. She became worse and died, three months after the onset of the first symptom. Her physician wrote that the spleen just before death was about one-half its previous size; no further blood-counts were made. No autopsy was done.

The case is a typical one of acute myeloblastic leukæmia, except for the aleucocythæmic blood condition. The counts prior to the patient's admission and while she was in the hospital were not elevated, and although no counts were made after her discharge, it seems unlikely that an increase of white cells would have coexisted with a decrease in the size of the spleen.

CASE II.—Chloroma. White woman, æt. 58, widow, housewife.

Complaint.—Tenderness of the teeth. Puffiness of the eyes.

Family History.—Negative.

⁶ Bramwell, B.: Brit. Med. Jour., 1902, I, p. 453.

⁷ Türk, W.: Wien. klin. Wchnschr., 1903, XVI, 1023.

Past History.—Usual childhood diseases. Scarlet fever at five years, followed by difficulty in hearing.

Present Illness.—Four years before admission, the patient consulted a physician for indigestion. Through routine examination, an enlarged spleen was found. At that time, the W. B. C. were 18,000, with 85 per cent of small round cells. Since that time, counts have varied between 9000 and 30,000, with mononuclears between 65 per cent and 90 per cent. The spleen was treated with X-ray, and arsenic was given. A little more than two years before admission, a swelling was noticed on the left cheek, just anterior to the ear. Soon a tumor appeared above the right clavicle. For several months at that time there was severe pain in the legs, especially in the knees. One dose of Salvarsan was given. About six months before admission several swellings appeared in the neck on both sides, and subsequently the other masses described in the examination developed. A few months before admission, there was excruciating pain in the teeth. Several teeth were extracted, some abscesses were found, and there was relief from pain in the teeth and knees. The patient's friends noticed that her complexion was becoming yellowish-gray. At the time of admission she had no especial complaint. She had lost 30 pounds in weight. Her hearing had become much less acute, though always impaired since scarlatina.

Physical Examination.—The skin was dusky, with an olive tint. There were masses on both malar eminences, invading the eye sockets. One of these masses measured 10 x 5 cm., and it was difficult to prove its connection with the bone. The other was smaller, firmer, and definitely attached to the bone. There was a flat mass connected with the left mastoid bone and extending downward to join matted nodules on the left side of the neck. She could hear nothing less than a shout. There was considerable thickening of the middle of the left clavicle. Glands were felt in the right and left axillæ; in the latter was a mass as large as the end of the thumb. Over the front of the chest were several subcutaneous nodules, to two of which the skin was attached. The inguinal glands were a little large on the left, not on the right. On the back were a number of small nodules, most of them in the skin. The surface of some of these had a somewhat grayish-brown color at the points where they were nearest the skin. They looked rather like old, discolored ecchymoses.

The gums were very tender about some of the exposed teeth. The heart and lungs were normal.

The liver reached to the umbilicus in the median line, and well below it on the right. The border was sharp and the surface smooth, with slight rounded prominences. The spleen reached about 7 cm. below the costal margin, was very firm and rather prolapsed toward the left.

Nothing abnormal was seen in the eye-grounds.

The Blood.—

Hgb. (Sahli)	66 per cent.
R. B. C.	3,928,000
W. B. C.	5120

Differential Count.—

	Wilson Stain.		Ehrlich Stain.	
	No. Counted.	%	No. Counted.	%
Poly. Neut.....	254	63.25	382	63.70
Poly. Baso.	0	0.00	1	0.17
Poly. Eosin.	23	5.75	34	5.60
Small Lymph.	62	15.50	128	21.30
Large Lymph.	33	8.25	41	6.80
Large Mono.	20	5.00	10	1.70
Transitionals	0	0.00	4	0.70
Neut. Myelocytes (?).....	6	1.50	0	0.00
Myeloblasts (?)	2	0.50	0	0.00
	400	99.75	600	99.97

There was slight anisocytosis of the red blood cells, no poikilocytosis, and neither basophilia, punctate or diffuse, nor nucleated forms. The polymorphonuclear forms frequently showed coiled, elongated nuclei, not unlike rare transitional forms. The convolutions of the nuclei were seen most clearly in preparations poorly (lightly) stained by Ehrlich's method. Some of the nuclei resembled tightly coiled snakes, and in some of them one end of the nucleus was separated from the coil and seemed actually to protrude from the cell. In some instances a very tightly coiled nucleus looked very much like a mononuclear cell, especially in a Wilson-stained preparation.

The Wassermann reaction was negative. The urine was negative and showed no Bence-Jones protein.

A few months prior to her admission the patient's physician sent a bit of tissue, containing a subcutaneous nodule from her body, to this hospital for diagnosis. A laboratory assistant made a section and destroyed the gross specimen; the stained section was forwarded to Dr. Winternitz who was away. His report follows:

"The section is from subcutaneous tissue, and bits of degenerated voluntary muscle occur between the lobules of tumor mass. The lobules are irregular in size and shape, and, as far as can be determined, do not represent a change in a preëxisting lymphoid structure but a new formation. This assumption is strengthened by the fact that several minute tubular structures occur in the very center of several lobules. These tubular structures are built by cubical epithelium and are only explainable by assuming that the tumor has infiltrated the deeper layers of the skin and surrounded some of the small glands and ducts, *i. e.*, the sweat-ducts of the skin.

Otherwise the tumor has a uniform appearance and consists almost entirely of a densely packed mass of small round cells similar to lymphocytes. In many places these overshadow the supporting framework of connective tissue and vessels completely.

In view of the history I should rather incline to regard this as a type of lymphatic leukæmia tending toward the aleukæmic variety with a tendency to nodule formation such as occurs in chloroma, mycetoma, etc. An absolute differentiation is, however, impossible from the section alone."

The patient left the hospital in the latter part of October, 1915, after two days' stay, and was again seen on April 2, 1916. In the interim she had had 36 injections of sodium cacodylate and eight X-ray treatments, one to the left side of the forehead, two to the back and the rest to the long bones. She had felt very well and had been quite active. Her chief complaint was of a neuralgic pain in the lower jaw.

Examination (April 2, Dr. Thayer).—The color was much better. The prominence which had been present on the left temple when last seen was entirely absent. There was still a slight prominence on the right forehead. The masses in the neck were about as before, but many of the nodules on the back had entirely disappeared. There were several nodules on the front of the chest. Although several of these were adherent, no definite discoloration of the skin could be made out. Three superficial masses in the skin, one just below the left breast and two below the right breast, showed a distinct slightly dirty gray-brown discoloration, just like that which was seen in the back on the previous examination.

The heart and lungs were clear.

The spleen was just about as before. The epitrochlear glands were palpable, the inguinals not essentially enlarged. The liver extended 12 to 12.5 cm. below the costal margin in the right mamillary line.

The patient's hearing was much improved. She could hear ordinary conversational tones.

The blood at this time showed:

Hb. (Sahli)	80 per cent.
R. B. C.	4,000,000 (+)
W. B. C.	7000 (+)

Differential Count (Wilson Stain), 200 Cells.—

Poly. Neut.	54.0 per cent.	
Poly. Baso.	1.0	"
Poly. Eosin.	6.5	"
Large Mono.	5.0	"
Small Mono.	27.5	"
Large Lymphocytes.	2.5	"
Transitionals	2.5	"
Myelocytes (Eosin.) ..	0.5	"
Unclassified	0.5	"
100.0 per cent.		

R. B. C. { Slight anisocytosis.
No poikilocytosis.
No basophilia.
Polymorphonuclears with
convoluted nuclei again
present.

The history of chronic splenomegaly, with leucocytosis and mononucleosis, the glandular enlargement and the many nodules of leucoblastic tissue left little doubt that the case was one of leukæmia. Certain features made the diagnosis of chloroma probable.

Chloroma is more common in individuals younger than this patient. The average age is about 20. Fifty-two years is the greatest age found reported. The onset of the disease is usually acute, often with pains in the knees, teeth or head. Hemorrhages, weakness and anæmia follow rapidly. Ulcerated gums and throat may lead to the diagnosis of Vincent's angina or diphtheria. There is usually exophthalmos, from invasion of the orbits by the chloroma tissue. Tumors form, showing a predilection for the periosteum of certain bones, especially of the face and skull. The order of frequency with which these bones are involved is: (1) Orbits. (2) Dura or sinuses. (3) Temporal bone. (4) Temporal fossa. (5) Sphenoid. (6) Ethmoid, etc. The nodules may be attached to sternum, ribs, lymphatic system, spleen, liver, subcutaneous tissue or kidneys. Pathological examination shows that there is practically no tissue or organ of the body which may not be infiltrated by chloroma tissue. The gross color of the nodules and of the infiltrating tissue is green. Sections of the tissue show lymphocytes and cells having the appearance of myeloblasts.⁸ The most characteristic blood cell has been described by Butterfield,⁹ and was thought by some to be pathognomonic of cases of chloroma, but it has often been seen in other cases of leukæmia. It is a non-granular mononuclear cell with a convoluted nucleus—a myeloblast. In cases of chloroma there are usually an enlarged spleen and liver. The course is almost always febrile, ending fatally in a few months. The longest case recorded lasted one and one-half years.

The case reported here was typical in the following respects: (1) The early pains in the teeth and knees. (2) The location of the tumors. (3) The color of the skin over the tumors, and

the generalized olive tint. (4) The enlarged spleen, liver and lymphatics. (5) The anatomical appearance of the excised nodule. (6) The anæmia. (7) The convoluted nuclei of the polymorphonuclear cells may have some diagnostic significance. The case was unique in these features: (1) The patient's age (58). (2) The chronicity of the disease (now four years). (3) The almost normal blood picture.

There are eight chief hypotheses as to the nature of chloroma. They embody two main ideas—one that it is purely a leukæmic disease, and another that it is purely sarcomatous. Various combinations of these central ideas have been advanced, into which it is scarcely necessary to enter at length. These various hypotheses are discussed by Lehdorff,¹⁰ from whom Pappenheim's views are quoted as follows: "Chloroma is a green-colored type of malignant hyperplasia of the hematopoietic tissue, which appears as hyperplastic chloroma or as chlorosarcoma, with all stages of intermediate forms."

It seems likely that the case reported here has more the nature of a neoplasm than of a blood disease; however, in view of the history of leucocytosis and mononucleosis, it seems not improbable that the case was studied during a remission and that definite leukæmic blood changes will appear before the disease has run its course.

CASE III.—Chronic Lymphatic Leukæmia. White man, aet. 60, married, farmer. Admitted April 3, 1916.

Complaint.—Indigestion. Weakness.

Family History.—Negative.

Past History.—Measles and pertussis in childhood. Pneumonia at 10. Erysipelas 10-12 years ago.

Present Illness.—In March, 1915, one year ago, he had an attack of "grippe" which lasted from six to eight weeks. He felt "weak and achy" until June. The skin became very tender and boils developed from the slightest injury. There was dyspnoea, which gradually increased until the time of admission. For three months before his admission, the patient had constant indigestion, without vomiting. He said he had had lumps under the left arm for 10 or 12 years. About six or eight months ago he noticed lumps in the neck, and in both groins about four months ago. He lost 30 to 40 pounds in weight. There was no oedema, and no purpura. There were many small boils from time to time, which ruptured and discharged bloody material.

Physical Examination (on admission).

There was marked emaciation. The skin was sallow, but lacked a lemon-yellow tint. There were a few pustules. The mucous membranes were quite pale. There was an occasional rather metallic cough, suggestive of mediastinal pressure. The teeth were very bad, many were carious, and there was a moderate pyorrhœa.

Glands.—The cervicals on both sides were enlarged, soft, discrete, and about the size of unshelled almonds. The axillaries were of similar consistency, but large—about the size of walnuts. The inguinal and epitrochlear glands were similar to the cervicals. In the right iliac fossa several rounded masses could be felt, which were thought to be glands.

Thorax and Heart.—Nothing unusual was found, except a rather loud systolic murmur at the heart's base, best heard over the right carotid artery. There was diffuse thickening of the radial vessels.

⁸ Burgess, A. M.: Jour. Med. Research, 1912, XXII, 133.

⁹ Butterfield, E. E.: Deutsch. Arch. f. klin. Med., 1908, XCII, 336.

¹⁰ Lehdorff, H.: Jahrb. f. Kinderheilk. u. Phys. Erzieh., 1910, LXXII, 53.

Liver.—This was felt three fingerbreadths below the costal margin in the midclavicular line; its edge was sharp but the consistency of the organ was about normal.

Spleen.—The spleen was felt deep in the flank, presenting a sharp edge and a notch. It moved with respiration, and lay two to three fingerbreadths below the costal margin.

The Blood.—The flow and clotting are normal.

R. B. C.....	3,128,000
Hb.	43 per cent.
W. B. C.....	7720

Differential Count (Wilson Stain), 250 Cells.—

Poly. Neut.	37.6 per cent.
Poly. Baso.	0.8 "
Poly. Eosin.	3.2 "
Large Mono.	5.2 "
Small Lymphocytes	50.0 "
Transitionals	2.4 "
Large Lymphocytes	0.0 "
Large Mononuclears with convoluted nuclei and granular protoplasm	0.8 "

100.0 per cent.

Slight anisocytosis and poikilocytosis of R. B. C. No basophilia nor nucleated forms.

Ewald Test Meal.—Negative except that there was seven per cent acidity deficit of free HCl. Total acidity was 20 ac. per cent.

Stool.—Negative.

Wassermann Reaction.—Negative.

Urine.—(Admission). S. G. 1.010. Alb. ++. Many pus cells. No blood. No casts.

Subsequently the pus disappeared from the urine, and the albumin was reduced to a trace.

April 8. X-ray treatment to spleen.

April 15. X-ray treatment to external glands.

April 17. W. B. C. 12,880.

Differential Count (Wilson Stain), 200 Cells.—

Poly. Neut.	59.0 per cent.
Poly. Baso.	0.5 "
Poly. Eosin.	1.0 "
Large Mono.	9.5 "
Small Lymphocytes	29.0 "
Transitionals	0.5 "
Myelocyte	0.5 "

100.0 per cent.

Many of the cells classed as polymorphonuclears have convoluted nuclei.

April 20. Temp. 103° F. Cough. Congestion of lung bases. Hb. 44 per cent. R. B. C. 3,224,000. W. B. C. 21,500.

April 23. W. B. C. 16,080.

Differential Count (Wilson Stain), 200 Cells.—

P. M. N.....	50.5 per cent.
P. M. B.....	0.0 "
P. M. E.....	0.0 "
Large Mono.	7.0 "
Small Lymph.	30.5 "
Large Lymph.	5.0 "
Transitionals	7.0 "

100.0 per cent.

Many polymorphonuclear cells have thick, tightly or loosely coiled nuclei and neutrophilic granules. Some nuclei are snake-like and so closely coiled as to suggest a mononuclear cell. Others have thick and elongated nuclei resembling transitionals.

April 25. X-ray treatment to external glands. The glands are all smaller than on admission, but at present are not quite so soft in the center as they were just after the first treatment.

April 27. Marked diarrhoea. Stools contain pus, no blood.

Stool Culture.—Hiss-Russell dysentery bacilli obtained. W. B. C. 36,080.

April 29. Some vomiting. W. B. C. 30,350.

Differential 200 Cells.—

P. M. N.....	41.0 per cent.
P. M. B.....	0.0 "
P. M. E.....	0.0 "
Large Mono.	0.5 "
Small Lymph.	58.0 "
Transitionals	0.5 "

100.0 per cent.

April 30. Dysentery and vomiting continue. Irregular, sharp elevations of temperature (highest 102.6° F.) alternate with sub-normal temperature. Dilatation of the stomach has set in. Definite "air hunger" to-day. CO₂ tension of alveolar air 22 mm. Hg.

May 1. Patient died.

The temperature ranged between 96° and 101° F. prior to the acute pulmonary infection of April 20.

Treatment.—X-rays to glands and spleen, Fowler's solution, Bland's pills, hydrochloric acid, and special treatment for dysentery and pulmonary symptoms.

An autopsy was done, and Dr. H. C. Schmeisser gave the following report, with plates:

AUTOPSY No. 4677. *Anatomical Diagnosis.*—

Primary.—(1) *Lymphatic leukaemia involving particularly lymph-glands and parenchymatous organs.*

(2) *Acute necrotizing and ulcerative colitis (Hiss Bacillus).*

Subsidiary.—Gastric ulcer. Fibrous pleurisy (rt.); pulmonary emphysema. Aplasia of left renal artery and atrophy of left kidney (congenital).

The body is that of a large-framed, emaciated, white man, 180 cm. in length. There is marked anæmia of the conjunctivæ, lips and tissue under the finger-nails. Many teeth are carious and there is some pyorrhœa alveolaris. The body shows definite evidence of emaciation. The eyes are sunken; the cheek bones are prominent; the clavicles project; the supra- and infra-clavicular fossæ are very deep. The skin over the whole body is loose and pale. The posterior cervical, axillary, inguinal and epitrochlear lymph-glands on both sides are greatly enlarged, moderately firm, discrete and freely movable between the skin and the deeper parts. The external surface of the body otherwise shows nothing of interest.

The *peritoneal cavity* presents a smooth, glistening serous surface throughout. Here and there are some fibrous adhesions. The margin of the right lobe of the liver extends 3 cm. below the costal margin in the right mammary line. The margin of the left lobe of the liver extends 5 cm. below the tip of the xiphoid. All the organs occupy the normal position, except for a slight displacement due to the large retroperitoneal and other lymph-glands.

The left pleural cavity is empty and presents smooth and glistening surfaces. The right pleural cavity is obliterated by fibrous adhesions.

The *thymus*, although carefully searched for, could not be demonstrated.

The *pericardial cavity* contains the usual amount of clear, straw-colored fluid. Its serous surfaces are uninvolved.

Heart.—Presents nothing of interest. The left myocardium on tangential section is uniformly reddish brown. The coronary arteries contain a few atheromatous patches. The root of the

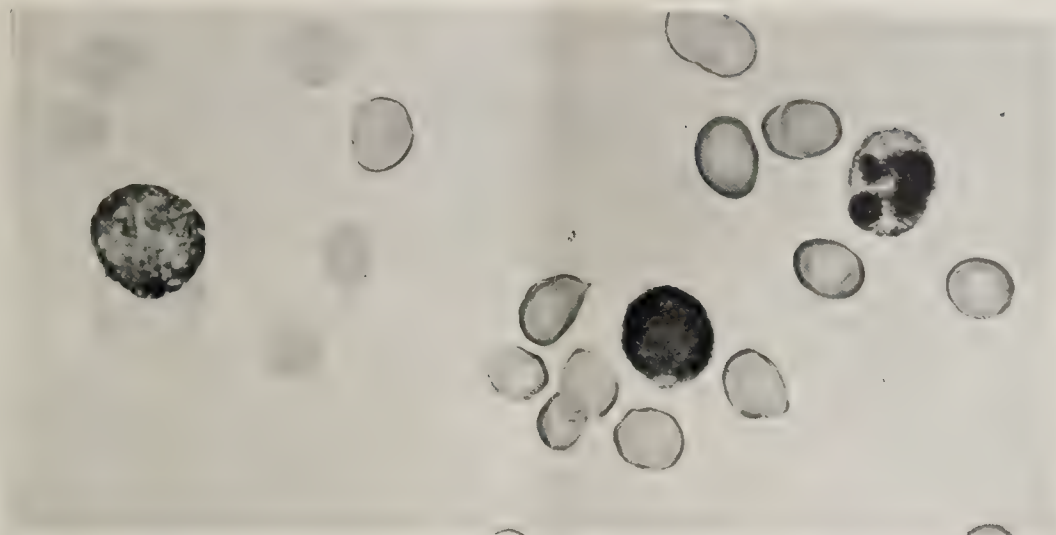


FIG. A. Blood of Case I ($\times 1000$). Showing 2 myeloblasts and 1 polymorphonuclear neutrophile.

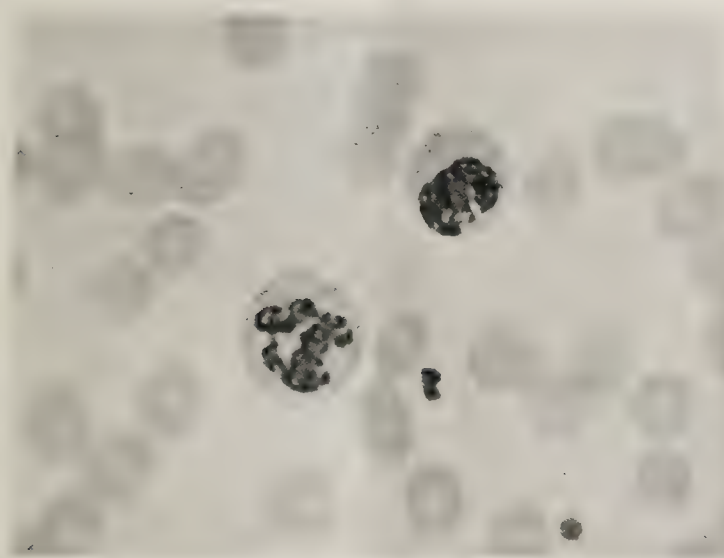


FIG. B. Blood of Case II ($\times 1000$). Showing young polymorphonuclear neutrophiles.

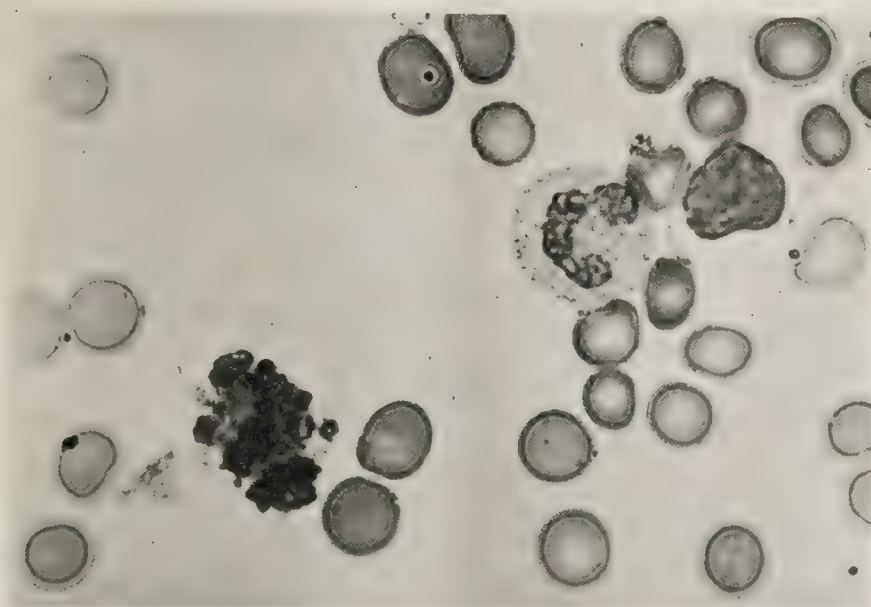


FIG. C. Blood of Case III ($\times 1000$). Showing lymphocyte, polymorphonuclear neutrophile and smudge.

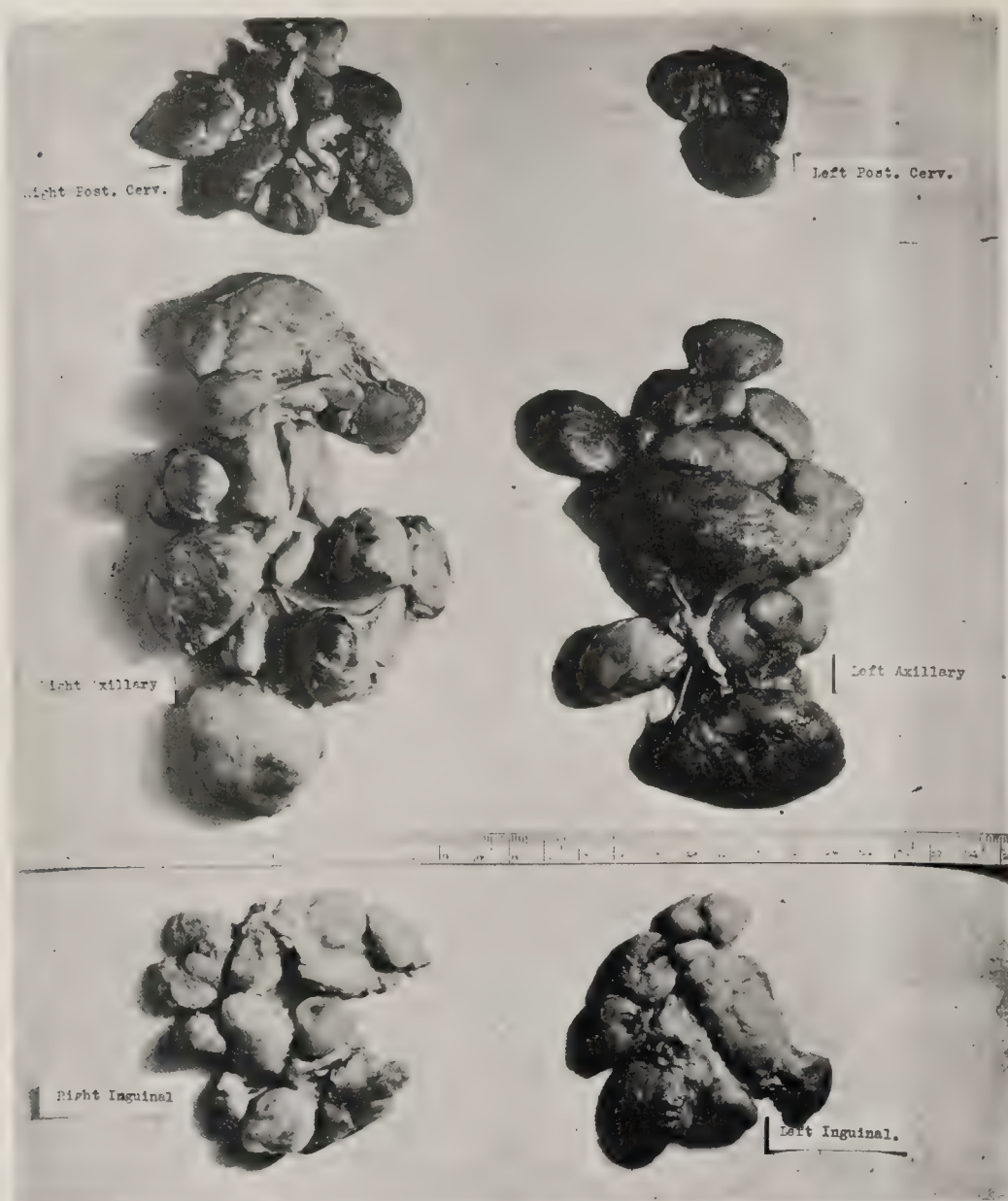


FIG. 1. Superficial lymph-glands. Note increase in size.



FIG. 3. (a) Retrothoracic lymph-glands. (b) Retroperitoneal lymph-glands. (c) Mesenteric lymph-glands. (d) A very large pancreatico-hepatic lymph-gland. (e) Pancreas. (f) Duodenum. (g) Mesentery. (h) Large vascular lymph-gland in region of the left adrenal and kidney.

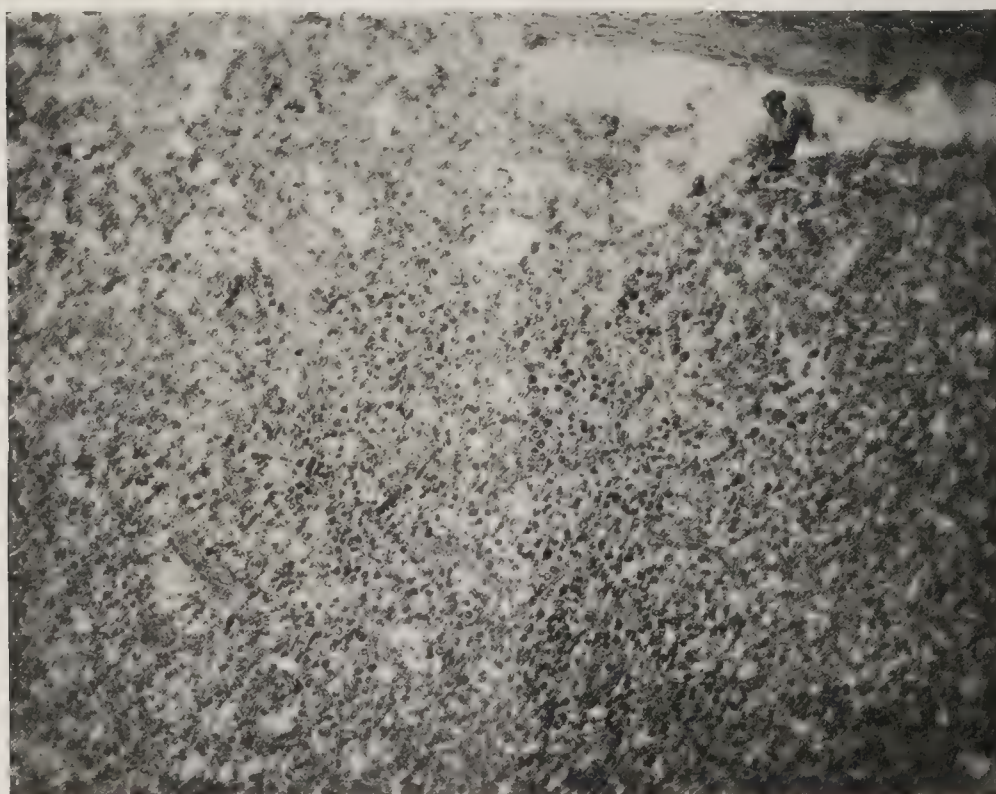


FIG. 2. Superficial lymph-glands. Note the diffuse hyperplasia of the lymphocyte with absence of follicles. The capsule is shown in upper right hand corner.

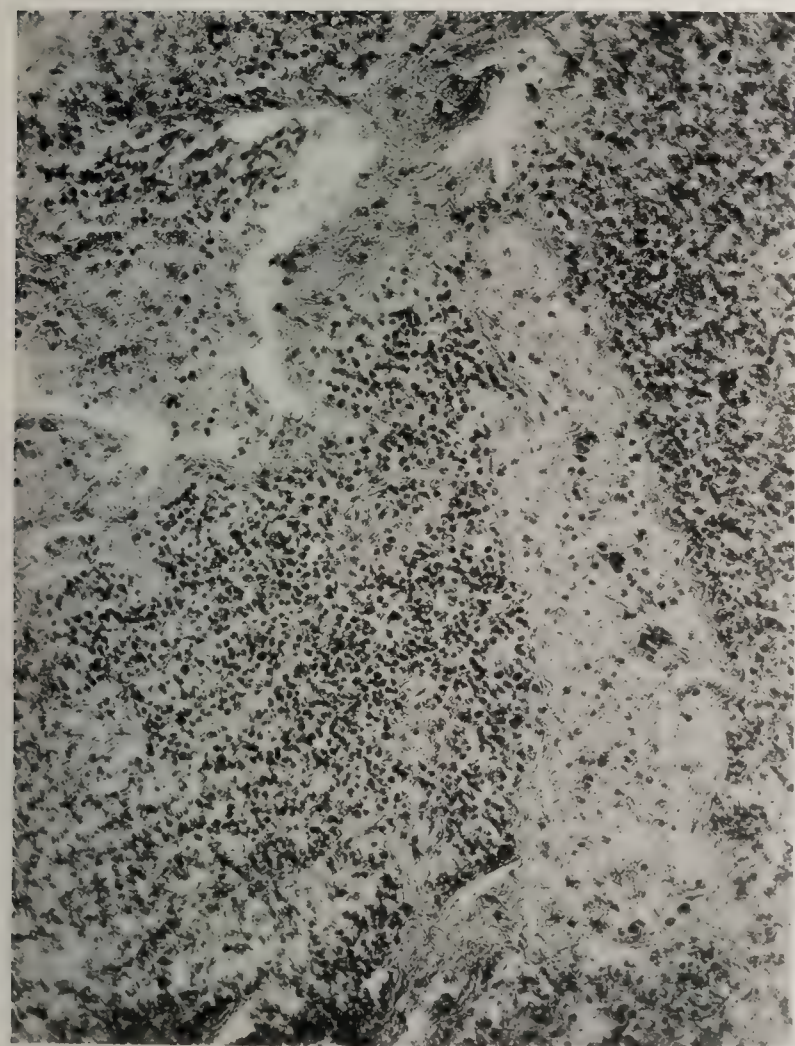


FIG. 4. Large lymph-gland in left kidney region. Note the very vascular, diffuse, lymphocytic hyperplasia with absence of follicles.



FIG. 7. Liver. Greatly enlarged. Note the characteristic periportal gray network.



FIG. 5. Spleen and right kidney. Note the increase in size of both organs and the characteristic gray granules of both surfaces of kidney.

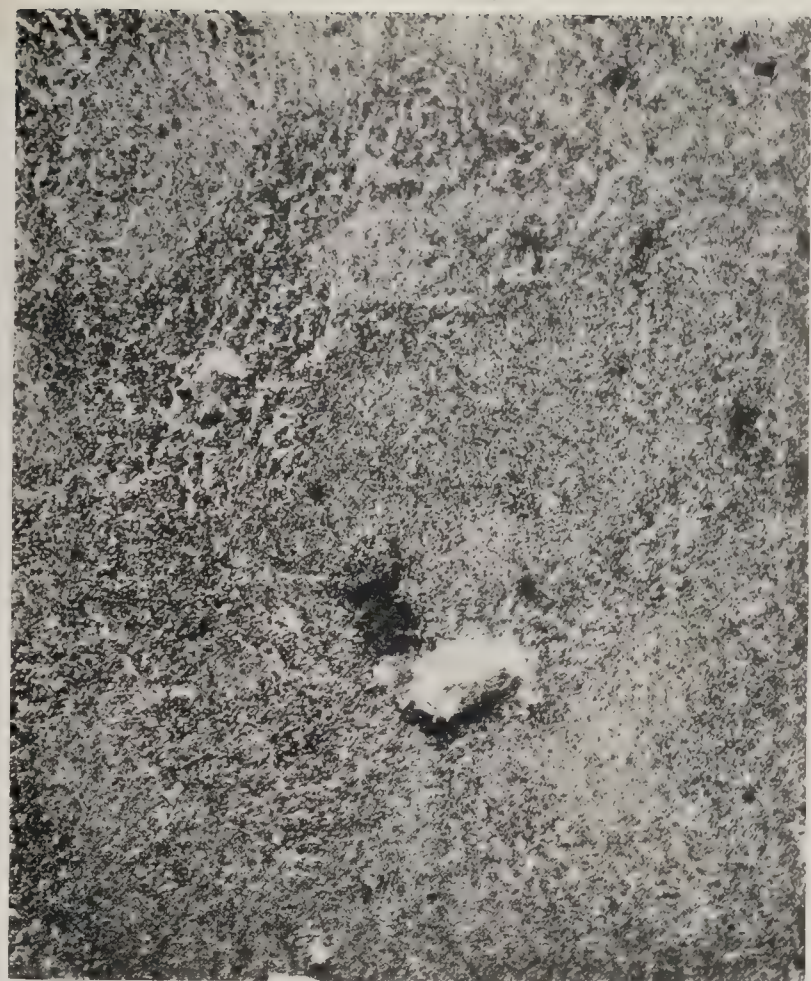


FIG. 6. Spleen. Note the hyperplastic Malpighian bodies.



FIG. 8. Liver. Note the hyperplastic peribulbar lymph follicles.



FIG. 10. Adrenal. Note the mass of lymphocytes in the medulla.

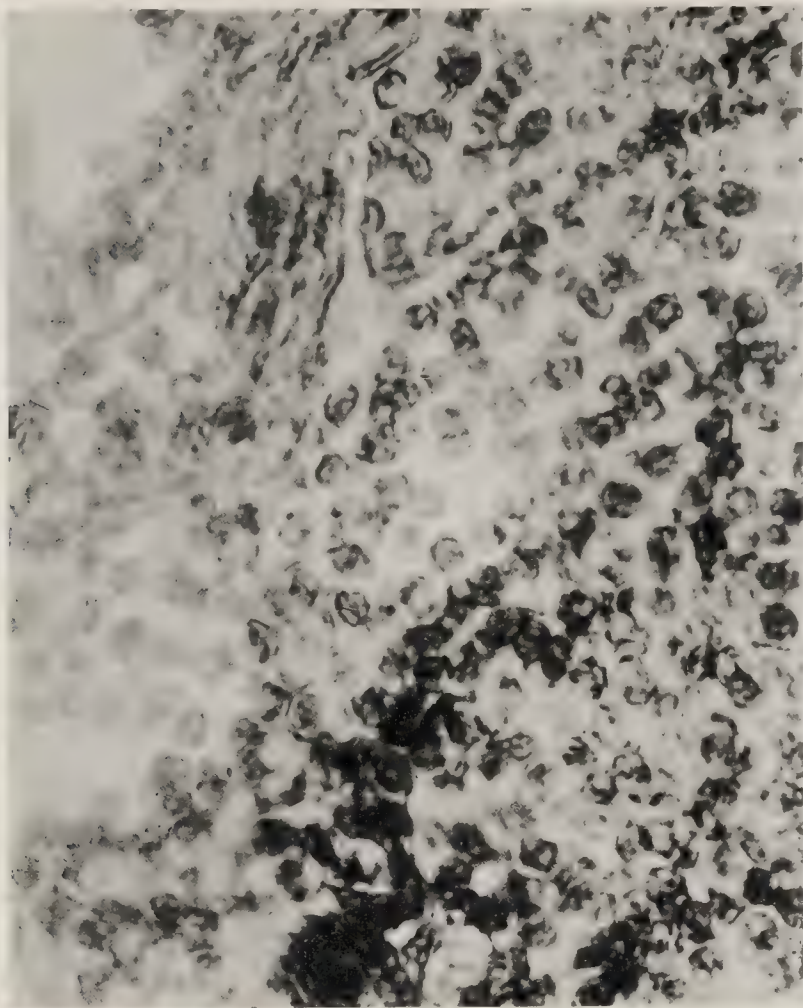


FIG. 9. Liver. High power of a peribulbar lymph follicle, to show type of cell (lymphocyte).

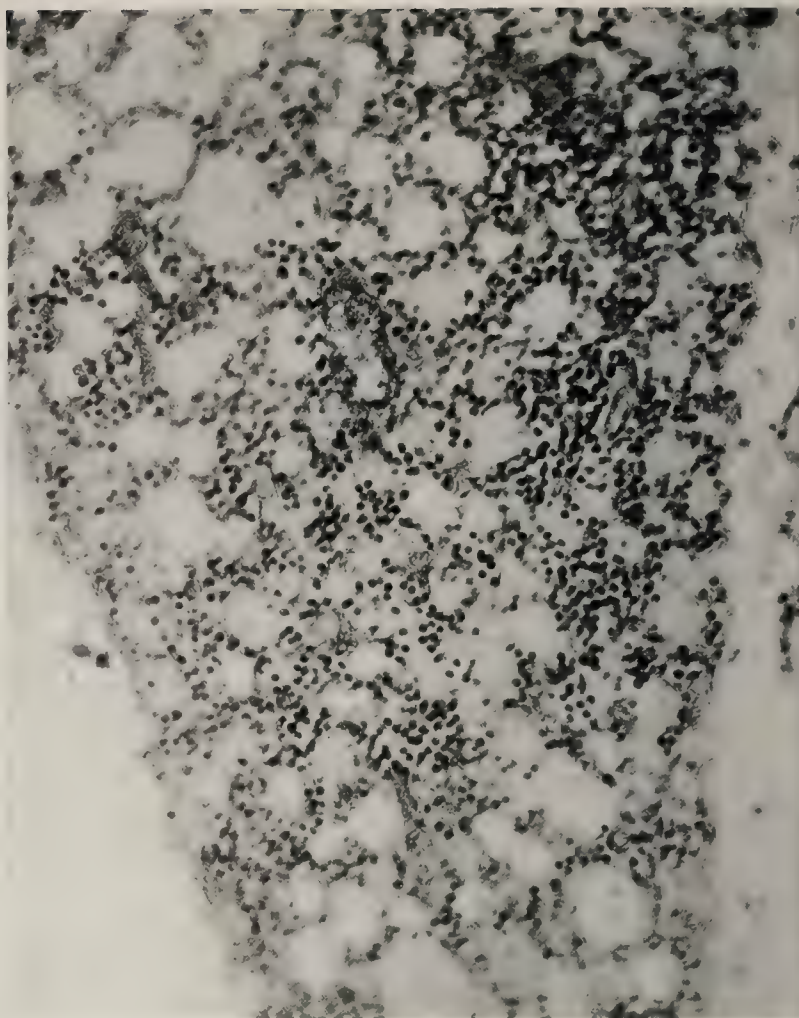


FIG. 11. Periadrenal fat. Note infiltration with lymphocytes.

pulmonary artery and aorta show here and there yellowish-white, opaque, slightly elevated patches.

Lungs.—Both lungs have practically the same appearance. They are large, pale, grayish pink and air-containing throughout, with large alveoli. On section, the surface is smooth, gray with unusually large air spaces. The bronchi, arteries, veins and the hilic lymph-glands present nothing of interest.

Spleen.—The *spleen* is greatly enlarged. It weighs 600 gm. and measures 18.0 x 13.0 x 5.5 cm. Its capsule is somewhat thicker than normal and of a slightly milky appearance. The spleen is practically normal in shape, except that its edges are more round. It is slightly soft. On section, the capsule and trabeculae are prominent; the Malpighian bodies are larger than usual. The pulp is reddish brown and does not rise or recede from the cut edge.

Stomach.—The *stomach* is of normal size and shape, and when opened presents nothing of interest except a small, superficial ulcer, about 0.5 cm. in diameter near the pyloric end on the posterior wall. Near-by, there is a slightly elevated, oval, gray area of about the same size. The duodenum externally and on section presents nothing of interest. The bile and pancreatic ducts are patent.

Pancreas.—The *pancreas* is of normal size and shape. It was not weighed but it measures 23 cm. in length. It has the normal yellow color, normal lobulations and consistency. On section, it shows the usual structure.

Liver.—The *liver* is very large. It weighs 2480 gm. and measures 30 x 22 x 9 cm. It is practically of normal shape except that its margins are slightly rounded. Its consistency is about normal. The capsule is delicate. Beneath it may be seen the lobulation. The center of each lobule is yellowish brown and the periphery is gray, forming a distinct network over the surface of the organ. On section, this lobulation is very pronounced and answers to the same description. The *gall-bladder* presents nothing of interest.

Adrenals.—The right adrenal weighs 6 gm. It is very soft. On section, its capsule and cortex present nothing of interest, but the medulla is scarce in amount and the cortical portions are separated, due to softening of the medulla. Left adrenal (see below).

Kidneys.—The right kidney is relatively larger than normal. It weighs 200 gm. and measures 13.5 x 7.5 x 4.5 cm. It is of normal shape and consistency. Its capsule is delicate and strips readily, leaving a slightly yellowish, granular surface. On section, the cortex is unusually wide, averaging 12 mm. The striæ are very distinct. The glomeruli can readily be seen as tiny bright red pin-points. Parenchymatous striæ are broad and gray. The striæ of the pyramids are also prominent. The pelvis and ureter present nothing of interest. Left kidney (see below).

Pelvic Organs.—The rectum, bladder, prostate, seminal vesicles and vas deferens present nothing of interest.

Intestines.—The small intestine throughout presents nothing of interest, but the cæcum and all of the colon excepting the rectum show extensive ulceration, most marked in their upper half. The ulcers are long and narrow, extending around the gut. They involve the entire thickness of the mucous membrane, undermining it, but seem to stop at the inner muscle layer. They are clean and show no reaction. The process is most marked; hardly half a centimeter of normal intestine remains between any of the ulcers.

Testicles.—Both testicles and epididymes are normal.

Lymph-Glands.—The lymph-glands of the retrothoracic and retroperitoneal regions and those which lie between the pancreas and the liver and those at the root of the superior mesenteric artery are very large, soft, juicy and mottled. They are gray, with splotches of bright red. On section, they are either of this appearance or are uniformly gray. One lymph-gland just above the pancreas, between it and the liver, is very large. It measures 8.5 x 5.5 x 3.0 cm. The largest of the retroperitoneal lymph-glands

measures 4.0 x 2.4 x 1.5 cm. The superficial lymph-glands, above mentioned, all present the same picture externally and on section. In addition to what has been said, they are uniformly gray in appearance both externally and on section. The axillary lymph-glands on both sides are the largest and most numerous. The largest on the right side measures 6.0 x 3.5 x 2.5 cm. The largest on the left side measures 5.0 x 3.5 x 2.5 cm. These superficial lymph-glands differ from the retroperitoneal and retrothoracic lymph-glands in that they seem to be less acutely involved. The left adrenal and kidney are buried in a red fluctuating mass.

After careful dissection of this mass, a normal appearing adrenal is exposed. The left ureter, which appeared normal externally, when opened, is traced into this mass of lymph-glands, and ends in a slight dilatation about 4 cm. long and 2 cm. wide. Along one side of the same is a zone, 2 cm. wide, of what appears to be renal tissue. This is all that can be demonstrated of the left kidney. The renal vein appears normal and can be traced to the inferior vena cava. The left renal artery at its origin from the aorta has a lumen of 0.2 cm., while that of the right renal artery is 0.6 cm. in diameter. The left artery has been cut across about 1 cm. from its origin. Its entry into the kidney pelvis cannot be demonstrated. (The above was considered to be a congenital atrophic kidney.)

Bone-marrow.—The bone-marrow, taken from the rib, appears grayish red and is moderate in amount.

MICROSCOPIC NOTES.

Heart.—Sections show a small mass of lymphocytes between the muscle fibers.

Lungs.—Moderate emphysema.

Spleen.—The Malpighian bodies are very large, otherwise they and the rest of the section show nothing unusual.

Stomach.—Sections from the ulcer show that it has undermined the mucous membrane at its edge and has extended to the first muscle layer. The mucosa and submucosa contain small masses of lymphocytes.

Sections of the gray nodule near the ulcer show an extreme infiltration of all the layers of the stomach wall with closely packed lymphocytes.

Pancreas.—The pancreatic tissue itself is not implicated, but the peripancreatic fatty tissue is infiltrated with lymphocytes.

Liver.—Sections show practically every periportal space to contain a mass of lymphocytes. The lymphocytes are limited to these follicles.

Adrenals.—Sections of the right adrenal show an infiltration of lymphocytes in a localized area of the medulla. These are also present in the periadrenal fat tissue.

The left adrenal and its periadrenal fat tissue are not implicated.

Kidneys.—Sections of the right kidney show small masses of lymphocytes throughout the cortex, frequently near blood-vessels.

A section of the left kidney taken through the dilated terminal part of the ureter, obviously the pelvis, and the zone, a few millimeters wide, of renal tissue adjoining it, shows the following picture: A wide zone of fibrous tissue with small masses of lymphoid cells, bordered on one side by mucous membrane with several layers of imperfect columnar epithelium. Just below this surface are occasional gland-like structures, also lined with several layers of columnar epithelium. This part of the section is rich in lymphoid cells. In other parts of the section are structures which appear to be greatly dilated renal tubules with cuboidal epithelium.

Prostate.—Sections contain extensive accumulations of lymphocytes between the muscle and fibrous tissue.

Intestines.—Sections from the small intestines show nothing abnormal. Sections of the large intestine taken through ulcers show the same to involve and undermine the mucous membrane, extending to the inner circular layer of muscle. The tissue at

the margin of the ulcer is necrotic and infiltrated with polymorphonuclear cells, red blood-cells, and in some sections with fibrin. The near-by blood-vessels are congested. A fibrino-purulent membrane covers the bases of some of the ulcers.

Lymph-Glands.—Sections from the following groups of glands were studied: bifurcation of the trachea, the right and left posterior cervicals, the right and left axillaries, the right and left inguinals, mesenteric, pancreatic-hepatic, retroperitoneal.

All these different glands presented the same histological picture. The normal histological structure into lymph follicles, medullar strands of lymph cells, lymph sinuses, etc., has been entirely replaced by a diffuse, closely packed mass of lymphocytes, uniform in appearance everywhere inside the capsule. The capsule in places contains small masses of lymphocytes. The latter are also in large number out in the periglandular fat tissue.

The large, red, juicy mass which pressed upon the atrophic left kidney has the same structure as the lymph-glands above except that it is more vascular.

Bone-Marrow.—Sections of marrow from the ribs show entire absence of fat. The lymphocyte is by far the predominating cell.

The clinical diagnosis was "chronic lymphatic leukæmia" (aleucocythæmic at first). This was borne out by the pathological findings. The case is clearly an instance of what Naegeli would call "Aleukæmic Lymphadenosis." He recognizes six types of this disease, but the one reported here belongs clearly to the most common and easily recognized group, the group with generalized lymphatic hyperplasia, frequently with qualitative blood changes.

An interesting feature of the case is the effect of the X-ray and the acute infections upon the blood-picture. After two X-ray treatments, without other apparent cause, the white cell count rose from 7720 to 12,880; the polymorphonuclears rose from 37.6% to 59.0%, and the lymphocytes dropped from 50% to 29%. The absolute number of polymorphonuclears

was greatly increased; the absolute number of lymphocytes was almost exactly stationary. At the onset of the pulmonary infection there was a definite increase in the total number of lymphocytes and a very slight polymorphonuclear increase. The dysentery was associated with a typical blood-picture of lymphatic leukæmia. During this infection the total number of lymphocytes was 17,503 per c. mm., and the polymorphonuclears numbered 12,443 per c. mm.

SUMMARY.

1. "Aleucocythæmic Leukæmia" seems to be a somewhat more satisfactory term to apply to those cases of leukæmia which show no increase of the total white blood-cell count than the commoner expressions, such as, aleukæmic leukæmia, aleukæmia, pseudoleukæmia, etc.

2. Fourteen of a total number of 105 cases of leukæmia on record at The Johns Hopkins Hospital were without leucocytosis at some time while under observation.

3. Three cases of aleucocythæmic leukæmia are reported in detail. One is a case of acute myeloblastic leukæmia, which went to a fatal termination, probably without ever having leucocytosis. The second is one of possible chloroma. It occurred in an elderly patient and was characterized by a chronic course, but the physical signs and the anatomical appearances in an excised subcutaneous nodule were very suggestive of chloroma. The third case is one of chronic lymphatic leukæmia, with a high mononuclear percentage, the blood picture of which was changed from that of an aleucocythæmic to that of a typical lymphatic leukæmia during an acute bronchitis and an acute bacillary dysentery.

OBSERVATIONS BEARING ON THE POSSIBILITY OF DEVELOPING AN EXPERIMENTAL CHEMOTHERAPY OF TUBERCULOSIS.*

By PAUL A. LEWIS, M. D.

(From the Henry Phipps Institute of the University of Pennsylvania, Philadelphia.)

It is a matter of record that, directly after his discovery of the tubercle bacillus, Koch devoted a great deal of attention to efforts to cure experimental tuberculosis in animals. Cornet,¹ then an associate of Koch, records the negative results of experiments with a certain number of drugs and chemicals in this endeavor.

The experiments made in this earliest work on the experimental therapy of tuberculosis naturally rested in large part on an empirical basis. The hope that an effective method of treatment could be arrived at in this way was based on no precedent. The materials chosen were naturally those that had some reputation as active agents in the treatment of tuberculous lesion in human beings.

It was a matter of course that a mind as logical as Koch's should have demanded the development of some more scientific basis for further experimentation. He proceeded on the tentative assumption that, if substances could be found with the capacity to check the growth of the tubercle bacillus in the culture flask, there might be those among them which would likewise restrain the proliferation of the parasite in the animal body. He accordingly carried out experiments with a large number of substances to determine their capacity to inhibit the growth of cultures. These experiments were not reported in any detail, either as to the precise methods employed or as to the quantitative aspects of the results attained. Koch² states that the following substances were especially active *in vitro*: "A number of ethereal oils, among aromatic compounds β naphthylamin, para-toluidin, xylidin; some so-called tar colors, namely fuchsin, gentian violet, methylen blue,

* Read before the Laennec Society, at The Johns Hopkins Hospital, March 27, 1916.

chinolin yellow, anilin yellow, auramin; among the metals, mercury in vapor form, silver and gold compounds. Gold-cyanogen compounds are especially striking in their surpassing activity over all other substances." Further: "All of these substances remained completely inactive when tested on the tuberculous animal."

In the course of these experiments it was found that a certain substance which could be extracted from the growing cultures was capable of profoundly influencing the progress of experimental tuberculous disease in guinea-pigs when administered to them during its course. In the first experiments the influence seemed to be of a curative nature and the substance, known at first as "Koch's Lymph," later as "tuberculin," was introduced into medical practice. What may be called the physiological activity of tuberculin is now a matter of common knowledge. Whether this activity can be so applied that the substance can be considered a useful therapeutic agent has been from the very beginning a matter of violent and almost fruitless controversy. As I have already pointed out elsewhere,³ any evidence which may be in favor of the usefulness of tuberculin in practical therapy is derived from clinical observation. This question is raised, not because it directly concerns the matter in hand, but because it is apparent that, as a matter of history, the discovery of tuberculin, the violent controversy that it excited and the brilliant discoveries in the field of serum therapy which followed so soon after, caused this early experimentation with well-defined chemical substances to be abandoned and for the time forgotten.

Then followed a period of 15 years, during which no observations of any interest in this field were recorded. Those interested in the disinfectant activity of various chemicals frequently included the tubercle bacillus in their lists of micro-organisms tested. The methods employed were not uniform and the chemicals were selected according to no general plan. As the chief result of present interest in the scattered work of this period, it has come to be recognized that the tubercle bacillus, as contrasted with other common pathogenic bacteria, is difficult to kill with chemical disinfectants. In this period there should be noted the paper of Boer⁴ on certain aspects of the activity of disinfectants. Working with a number of non-related substances, he found that there were certain differences in the intensity of the action of various substances against cultures of non-related species of bacteria.

This concept was developed further and practically applied to the differential cultivation of more closely related species by Loeffler, Conradi, and others. It was found that various anilin dyes, malachite green in the first instance, cresyl violet, crystal violet and basic fuchsin in later cases, markedly check the growth of *B. coli* or various troublesome micrococci in concentrations which do not inhibit the growth of *B. typhosus*.

To substances showing this type of differential activity Bechold and Ehrlich⁵ applied the term partially-specific (*halb-spezifische*) disinfectants in contradistinction to the more highly specific bacteriolysins of the blood serum of immunized animals. These authors applied the highly complicated methods of synthetic organic chemistry to the development of

a series of closely related chemical compounds whose disinfectant activity they then studied from this point of view. Their studies revealed the most striking examples of this partially specific disinfectant action. For instance, tribromnaphthol was found to possess a very strong disinfectant action against staphylococci, streptococci and diphtheria bacilli, very little against *B. pyocyaneus* and none at all against the tubercle bacillus. Monochloronaphthol is more active against staphylococci than cresol, but far less active than tribromnaphthol. Against the pyocyaneus and the tubercle bacillus, on the contrary, monochloronaphthol is very active.

The early efforts of Ehrlich to develop chemotherapeutic agents for use in experimental trypanosomiasis were much influenced by the thought that test-tube study of the disinfectant action of substances against the parasite could be used as a clue to the chemicals which it would be profitable to study subsequently in animal experiments. The expectation, in these instances, proved without foundation and in fact the substances more active *in vivo* often had very little activity in the test-tube. It would probably be short-sighted to conclude from this experience in a very special field that test-tube results could never be useful as a guide. And in fact, the recent observations (after the fact, so to speak) of Schiemann⁶ show that salvarsan, inactive in the test-tube against protozoa, but very active in the body, is active in the partially specific sense against certain bacteria, both in the animal body and in the test-tube.

The hope, so evidently entertained by Koch, that it would be possible to develop in a rational way specific chemical agents to cure particular diseases (tuberculosis first of all in his mind), fulfilled in the most spectacular way by Ehrlich at a time when it had been abandoned as a moving conception in the minds of most workers, has again become a dominating factor in many laboratories where tuberculosis is a subject of study. The general considerations which must be taken into account when the principles developed by Ehrlich are applied to the study of tuberculosis have been well stated and at length by Wells⁷ and his associates, and need not be further discussed here. We reiterate, for the sake of emphasis only, that the methods of handling tuberculosis experimentally and the conception that it might be possible by systematic search to find a rational treatment we owe to Koch. The model for such a search, the realization of the vast labor by a highly complex organization which must be contemplated as probably essential to achievement, and finally, the demonstration that for one radically different but equally tenacious disease (syphilis) success along these lines is possible, we owe to Ehrlich.

It may be profitable to consider briefly in more detail what is involved if we are to try, with hope of success, to apply the principles of Ehrlich to tuberculosis research. In the first place, Ehrlich's success was in no small measure due to the fact that he had to deal with experimental diseases whose course was rapid and whose limitations were very precise. From the time of infection to certain death in the untreated animal was in his typical case three or four days, and the exact condition of the animal could be determined at any moment by a simple examination of the blood. In our case we have no

such favorable basis for experimentation. In laboratory animals infected with properly selected cultures, death is certain, but the length of life is very uncertain except after most overwhelming doses, and I know of no experiment which can be terminated in less than a month. Many require much longer before an interpretation is possible.

Before this Society, four years ago, I reported observations on experimental tuberculosis of the cornea made with the cooperation of Dr. Montgomery,⁸ which we hoped would give a good basis for therapeutic tests. This lesion is useful for the study of certain features of the disease but fails in other very important particulars. Much further work is needed to develop conditions under which the generalized disease or local lesions will run a precise and invariable course. It is not to be expected that high speed will be attained, but the shorter the course the more useful will be such a reaction as a basis for work.

On the other hand, tuberculosis is a field of study offering certain distinct advantages. The bacteria are demonstrated in the tissues with comparative ease and certainty; in the tissues they cause a very distinct local lesion; and the distribution of certain chemicals to this diseased tissue can be very precisely followed.

This last factor, the distribution of drugs to the tissues, has been the starting-point for a number of recent researches, and for some premature efforts in the treatment of the human disease. Our own recent work has been very greatly influenced by the observation that certain anilin dyes, when injected into the living tuberculous animal, become concentrated to a considerable extent in the diseased tissues. On the occasion of a visit to Baltimore four years ago, to attend a meeting of the Society, I was shown some very beautiful preparations by Dr. Winternitz, preparations made in a study of the origin of the cells taking part in the reaction of the earliest hours after an infection of the animal with tubercle bacilli, and since carefully described by Bowman, Winternitz and Evans.⁹ My interest was aroused in the possibility of making a wider application of the so-called vital stains, and I soon found by experiment that the fibrocaseous tubercle took up these stains in a characteristic way. The results of these early experiments were recorded and summarized in the following terms:¹⁰

The first of these experiments shows again the selective action of Isaminblau for the large mononuclear phagocytic cell as pointed out by Goldman. These cells are found abundantly in the peripheral portions of fibroid tubercles.

The second experiment is of great interest, showing, as it does conclusively, that extraneous chemical substances of proper constitution may within a few days penetrate to the caseous center of a tuberculous mass and become concentrated there in greater degree than in the normal surrounding tissues. The particular substance used in this experiment, Trypan-rot, may probably be without effect on the lesion itself, but the result should be a great stimulus to future work in a similar direction.

These experiments have seemed to us of the utmost importance as a basis for further experimental work of a co-ordinated chemical and biological nature. The opinion had been quite generally expressed that, since the tuberculous tissue was with-

out an internal blood supply, it could be reached only with difficulty, if at all, by medicinal agents which might be made to circulate in the blood stream. Such an opinion, if of decisive weight, would make it appear to be an unreasonable waste of time to experiment to any great extent with the idea of developing general medicines that might be hoped to influence the local tuberculous process. The actual result, on the contrary, rendered such experimentation reasonable and, as it seemed to us, eminently desirable.

Before dealing in greater detail with our subsequent work on this subject, I wish to refer briefly to certain observations of others. Independent observations by De Witt¹¹ in this country and by von Linden¹² in Germany have shown that when methylene blue, or any one of several of its modifications, is introduced into the living diseased animal, the leuko-base of the dye is to be found in the caseous portions of the tubercle. Since methylene blue strongly restrains the growth of the tubercle bacillus outside the body (von Linden claims that the leuko-base is more strongly germicidal for the tubercle bacillus than the dye itself), and since, moreover, von Linden asserts that the tubercle bacillus is stained in the lesions, it would seem that nearly all the desirable qualities that could be postulated for the object of our search are possessed by this dye. Suffice for the moment to say that the work of von Linden is considerably offset by criticisms offered by her colleagues and former associates, and that De Witt's results are not in accord with it in many important particulars. For the past four years the work of Dr. De Witt and Dr. H. J. Cooper in the laboratories of the Sprague Memorial Institute, Chicago, under the direction of Dr. H. G. Wells, has followed the same general course as the work in the laboratories of the Phipps Institute. As we have used quite different materials, the two series of researches are to be considered as complementary.

Returning now to the progress of our own experiments, I would call your attention to the obvious, and say that the further development of such a subject as this is dependent on the pursuit of both chemical and biological studies in a carefully co-ordinated way. I have been fortunate in having as an associate Mr. R. B. Krauss, and throughout the rest of the paper, whenever points involving chemical manipulation are referred to, the work is to be credited to him.

The first concrete problem outlined on the basis of the above experiments was to take the dye "Trypan-rot," which had been used in the more striking of the experiments above commented on, and try by chemical manipulation to form from it or with it a substance having physiologic activity while preserving the qualities which enabled the dye to penetrate the tubercle.

Mr. Krauss undertook to make as many modifications of trypan red as he could, following certain general lines.

1. The staining qualities of the substance were to be at least in part preserved.

2. The preference was to be given to substances containing iodine, phenolic substances, or certain other constituents.

These specifications were drawn up on very general grounds, some of which may be stated as follows: Iodine was selected

because of the long-standing belief among medical men that iodine had some influence unfavorable to the progress of tuberculosis when applied locally either as an element or as iodoform; carbolic acid, guaiacol and other phenolic substances were known to be relatively active disinfectants against the tubercle bacillus, and some of them also enjoyed a reputation as medicines for this disease. The staining qualities were to be preserved as far as possible as a guide to the localization in the course of the subsequent animal experimentation.

The chemical work was successful. In the course of a year and a half about 75 compounds were secured on the plan outlined. The chemical manipulations and results have been published by Krauss.¹³ These preparations were used in a preliminary way in animal experiments, and some interesting observations were made. In general it was indicated that none of the substances exerted any curative influence on experimental tuberculosis. Some of them seemed, however, to have a definite influence on the vigor and rate of the formation of blood vessels and connective tissue in and around the tuberculous process; the tests being made on the cornea of the rabbit.

The plan had been to prepare enough of each substance for a moderate amount of preliminary experimentation and then to make some more of those which seemed useful for further work. About the time the preliminary study of these compounds was completed, the war began and necessitated a change of plan. We had been purchasing trypan red from abroad and a further regular supply was unobtainable. What was on hand and the occasional lots since secured we have used in a study of the composition of the substance with view to its manufacture.

Trypan red was first made for Ehrlich and was assigned a definite chemical formula by him, presumably based on the method of manufacture. On the basis of this formula the manufacture of the substance should be relatively easy, but we have not succeeded in carrying it out. On the contrary, we have been able to show that the trypan red of the German market does not agree with its constitution as given by Ehrlich. Only by continued analyses can we hope to learn how to make the substance. Under the present circumstances the work we have done in this particular field cannot be used to advance the subject until we are able to repeat our experiments with certain of the preparations and do it in such a way that they may be susceptible of repetition by others. I have reason to believe that these difficulties will be overcome in due time. We have meanwhile been searching for some other substance which might have the essential properties of trypan red and which at the same time could be made by us.

Following our observation that the tuberculous tissue in the living animal was easily penetrated by trypan red, many other dyes of the same general class, chemically speaking, were tested for their reaction in this particular. A considerable number were found which could become concentrated in the diseased tissue to a greater or less extent. Many of these had never been accurately described from a chemical point of view; others presented difficulties in manufacture beyond our means. After much consideration, a dye known to the trade as Niagara blue 2B (Benzidin + 2 H. Acid) was chosen as the starting-

point of a second attempt to construct a series of iodine and phenol compounds. Owing to the state of the chemical trade it has been necessary for us to build up this substance from the raw products. This has now been accomplished on a scale adequate for the purposes of our work, and we have recently had available a small series of finished compounds for further biological study. It is unlikely that these substances will replace those made with trypan red, but they are fully as likely to be instructive, and we now have the assurance of a solid foundation for the work.

Covering about the same period of time as these studies on the relation of the vital stains to the diseased tissue, and in the hope of acquiring information which should in some measure guide that work, we have been studying the disinfectant action of various substances for the tubercle bacillus. We have hoped to discover more substances having the partially specific action discussed in the earlier paragraphs of this paper. Much time has been spent over methods. The procedure by which the results here reported were obtained was to determine the least concentration of the substance in glycerin-bouillon which would definitely inhibit the growth of the tubercle bacillus. For comparison, from the side of the bacterial species we have used so far chiefly the typhoid bacillus, determining in the same way the concentration of the substance required to prevent its growth in the same medium.

Because of the relation to the work outlined in considering the subject of the vital stains, we have so far paid particular attention to anilin dyes. We have also considered the more common disinfectants and certain substances which are used in the building up of dyes.

Certain rather striking observations have been made, which may be briefly recorded here. We hope to publish shortly a report covering the examination of several hundred substances by this method.

I. PHENOL (CARBOLIC ACID).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/800	No growth	No growth
1/2000	Good growth	No growth
1/4000		Good growth

II. RESORCIN.

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/1000	No growth	
1/2000	Good growth	No growth
1/4000	Full growth	Mod. growth
1/20,000		Good growth

III. No. 158—BROWN DYE MADE BY COUPLING BENZIDIN AND RESORCIN.

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/200	Mod. growth	
1/400	Full growth	
1/20,000		Very slight
1/40,000		Mod. growth
1/100,000		Mod. to full growth

IV. ACRIDIN ORANGE. (DYE WITH ACRIDIN AS A BASE).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/2000	No growth	
1/4000	Full growth	
1/100,000		Slight growth
1/200,000		Mod. growth
1/400,000		Full growth

V. HELIOTROPE (KALLE & Co.) (A DYE RELATED TO SAFRANIN).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/1000	No growth	
1/2000	Very slight	
1/4000	Mod. growth	
1/10,000	Full growth	
1/400,000		No growth
1/1 million		Mod. growth
1/2 million		Mod. growth
1/4 million		Full growth

Taking from these tables the concentrations at which the effect on growth appears to be equal, and considering the susceptibility to the action on the part of the typhoid bacillus as unity, the following figures for the susceptibility of the tubercle bacillus are obtained:

Phenol. Typhoid 1/800 = T. B. 1/2000 or susceptibility of T. B. = 2½.

Resorcin. Typhoid 1/4000 = T. B. 1/100,000 or susceptibility of T. B. = 25.

No. 158. Typhoid 1/400 = T. B. 1/100,000 or susceptibility of T. B. = 250.

Acridin Orange. Typhoid 1/4000 = T. B. 1/400,000 or susceptibility of T. B. = 100.

Heliotrope. Typhoid 1/1000 = T. B. 1/400,000 or susceptibility of T. B. = 400.

These striking instances serve to illustrate the simplest phase of the problem. The data so far collected for consideration make certain more general statements possible.

(a) Of the anilin dyes, this partially specific activity is manifested quite generally by those related to safranin and to acridin. It is shown in greater or less degree by many of the azo-dyes made with benzidin as the basic constituent. On the whole the number of substances showing this property is large rather than small.

(b) Although in the studies previously made with other bacteria, the concentration required to inhibit the growth of the culture is roughly proportional to the higher concentration required to kill the microorganism in a short period of time, with the tubercle bacillus this is not the case. So far we have discovered no substance by which the tubercle bacillus is killed more readily than is the typhoid bacillus, and while we have used the term "partially specific disinfectants" in recognition of the work of others along similar lines, it would be more nearly correct to speak of partially specific inhibitors of growth.

(c) The ability to inhibit the growth of the tubercle bacillus in cultures is not dependent on high disinfectant activity in general, and is an attribute of a number of substances which are relatively non-toxic for higher animals.

In conclusion, I feel that the results described in the preceding pages form a substantial foundation for future work. With the localization of the dyes in the centers of the masses of tuberculous tissues and in certain cells in the peripheral portions of the same, the problem of distributing extraneous chemical substances to the diseased tissues was solved in its grosser aspects. It is equally clear that relatively non-toxic substances may be very active in restraining the growth of the tubercle bacillus outside the body. It may be predicted with a

fair degree of assurance that there will soon be at hand a number of substances which can be concentrated in the diseased tissue, and which will at the same time possess in considerable degree the ability to restrain the growth of the tubercle bacillus in cultures. This we are disposed to think will mark a distinct step in advance toward the solution of the abstract problems involved in the development of a specific therapy for tuberculosis as contrasted with our position of five years ago.

Will it mark a long step toward the practical treatment of tuberculosis? It is unlikely. There is still no scientific observation to guide us further toward a substance having these qualities and also capable of coming into effective contact with the tubercle bacillus in the body tissues and fluids, considered minutely.

It should also be fully recognized by everyone concerned that the practical problem of treating tuberculosis may be a far more difficult thing to accomplish than its laboratory prototype. Certainly it will be a most unfortunate thing for the progress of tuberculosis research if every substance showing interesting properties in the laboratory is immediately rushed to the clinic regardless of consequences. In this situation, patience is to be taken more than usually as an evidence of virtue.

LITERATURE.

1. Cornet, G.: Ueber das Verhalten der Tuberkelbacillen im tierischen Organismus unter dem Einfluss Entwicklungshemmender Stoffe. *Ztsch. f. Hyg.*, 1888, V, 98.
2. Koch, R.: Ueber bakteriologische Forschung. *Verh. d. X. Internat. Med. Kong.*, 1890-91, I. Berlin; *Gesammelte Werke von Robert Koch*, VI, 659.
3. Lewis, P. A.: The Pathological Basis for the Use of Tuberculin. *Jour. of Outdoor Life*, Jan., 1912.
4. Boer, O.: Behring. *Gesammelte Abhandlungen*, Leipzig, 1893, 198.
5. Bechold, H.: Desinfektion. *Paul Ehrlich's Festschrift*. Jena, 1914, 505.
6. Schiemann, O.: Weitere Untersuchungen über die Wirkung Chemotherapeutischer Mittel in Vitro. *Ztsch. f. Immunitätsfrag.*, 1914, XXIV, 167.
7. Wells, H. G., De Witt, Lydia, and Cooper, H. J.: Studies on the Chemotherapy of Tuberculosis. *Reprints of Sprague Memorial Institute*, Chicago, II, 1.
8. Lewis, P. A. and Montgomery, C. M.: Experimental Tuberculosis of the Cornea. *Jour. Exp. Med.*, 1914, XX, 269.
9. Bowman, Winternitz and Evans: Ueber die Vitalfärbung des Tuberkels. *Centralbl. f. Bakt.*, I. Orig., 1912, LXV, 403.
10. Lewis, P. A.: The Selective Relation of Certain Vital Stains to the Tubercle. *Arch. of Int. Med.*, 1912, X, 68.
11. De Witt, Lydia: Preliminary Report of Experiments in the Vital Staining of Tubercles. *Jour. of Inf. Dis.*, 1913, XII, 68.
12. Linden (V.): Beiträge z. Klin. d. Tuberk., 1912, XXIII, 201.
13. Krauss, R. B.: The Preparation of Compounds of Trypan red with Iodin and other Substances. *Jour. Am. Chem. Soc.*, 1914, XXXVI, 961, 1914.

DISCUSSION.

DR. FORD: I do not feel that I am in a position to say very much about work of this character, which so manifestly has consumed many hours of energy, and such extended intellectual effort. Dr. Lewis's paper is a great surprise to me in some respects. I do not think that *a priori* any of us would have expected the tubercle

bacillus to be more sensitive to disinfectants than are other organisms. This calls to my mind the controversies which existed for some time after the bacillus was discovered. You may remember that the granular bodies that appear in the bacilli were first interpreted as spores. The proof that they are not spores rests upon their low thermal death point and upon the fact that the tubercle bacillus is not so resistant to disinfection as are organisms that produce spores. There are a number of phenomena suggesting that the tubercle bacillus is not destroyed at a temperature below 75 C. Other indications are that the thermal death point is 60 C., as for the ordinary non-sporulating bacteria. The matter was settled by Theobald Smith in experiments in which he showed that there had been certain fundamental errors in the observations of previous workers, and that if you took the tubercle bacillus and determined its thermal death-point with due regard to the fact that it is necessary to disinfect all parts of the tube, if you avoid all errors, the tubercle bacillus is found not to resist any greater degree of temperature than organisms like the typhoid or the color bacillus.

I do not think that anyone imagined that the tubercle bacillus was going to prove more sensitive to the action of drugs than are ordinary bacteria. In this connection Prof. Phelps of the Public Health Service demonstrated that, in ordinary disinfection, there are always some organisms that survive for long periods of time, and he regards disinfectants as acting according to chemical laws.

I do not recall whether Professor Phelps's work has even been confirmed or not. There are, however, some interesting things which have some relation to it and which tend to confirm it. If, for instance, you attempt to determine the action of heat upon milk and estimate the number of bacteria in milk and try to find the point at which all bacteria are destroyed, you find yourself beset with countless difficulties. You cannot easily find the point at which all bacteria are destroyed, and if you plot out your results, you get a curve like the one obtained by Professor Phelps with the disinfectants. In the same way Sedgwick and Winslow found that the destruction of bacteria in ice followed the same sort of curve. I do not know that this is any explanation of the points that Dr. Lewis has suggested, but it is analogous.

In connection with what Dr. Lewis said about the action of dyes immediately after heating, it is interesting to know that one sometimes gets similar reactions in saponin. If you heat your solution of saponin to determine the thermal death-point, you do not always find it, but the tubes which have been heated seem to be much more hæmolytic than the saponin was before it was heated.

Finally, it is very interesting to recall the influence of Ehrlich upon this work. After all, most of our studies in regard to disinfection followed along a certain level up to the time of Ehrlich's work, but since then we have had an entirely new series of observations which are extremely important.

NOTES ON NEW BOOKS.

Hygiene and Sanitation. By SENECA EGBERT, A. M., M. D. (Philadelphia: Lea & Febiger, 1916.)

The sixth edition of Egbert's *Hygiene and Sanitation*, published by Lea & Febiger, is a compact and comprehensive manual of about 500 pages, which deals exclusively with subjects bearing upon public health questions. In this edition a successful attempt has been made by the author to bring the subject matter up to date, although some of the older theories and earlier views are retained.

The addition of a new chapter upon Industrial Hygiene and Occupational Diseases is a clear response to the growing public appreciation of the importance of social hygiene.

The subject matter of the manual is divided into 16 chapters, each one of which takes up a subject of vital importance to public health. The subject matter is clearly presented without any unnecessary complications from the use of technical or medical terms. It should prove of great value to the general practitioner of medicine who has little time to go deeply into the subject of hygiene and who will find in this book concise and exact descriptions of the most important topics in sanitary science. It should also prove valuable to the medical student, since it will afford him the requisite information in a brief space, with accurate references to more extensive treatises on the subject. Finally, the non-medical man, the sanitary and the scientific student, should find the publication extremely helpful because of the simplicity of presentation.

W. W. F.

The Criminal Imbecile. By HENRY HERBERT GODDARD, M. D. (New York: The Macmillan Company, 1915.)

The aim of Dr. Goddard's book—to "help the lawyer make a more successful defense of the imbecile criminal, the judge to dispense justice to this much misunderstood class of high-grade imbeciles, and society in general to realize its responsibility for the mental defective"—is certainly a laudable one, and to this end the material is presented in an interesting, simple, and logical manner, and the discussion is pertinent.

Details are given of three murders committed by as many high-grade imbeciles, and following this are chapters on "The

Criminal Imbecile," "Responsibility," and "Punishment." In conclusion we find appendices full of bewildering legal hypothetical questions and lawyers' charges, which are eloquent proofs of the need of revision of the existing laws that deal with the mentally abnormal criminal.

The three murders were committed by youths belonging to a class that ordinarily floats along undetected in society, but which on skilled examination proves to be high-grade imbecile in its mentality and adaptation. The cases are unusual because of the use in court of the Binet-Simon tests as legal evidence of the prisoner's inferior mentality.

In the chapter on "Responsibility," Dr. Goddard feels that children or defectives with a mentality of 12 years or under do not know much about right and wrong, and that the imbecile knows the nature but not the quality of his act.

In regard to punishment the author sanctions life commitment to an institution for defectives or even a state prison. In connection with this point the broader and more fundamental problem of preventing imbeciles from becoming criminals is taken up, and emphasis is laid on the importance of early recognition and supervision of defective states. The chapter concludes with a plea for the study of defective school children with especial reference to reducing the birth-rate of these individuals and preventing further propagation—the root of the whole problem.

The book can well be recommended to physicians as well as to lawyers and laymen, and Dr. Goddard is to be commended for the production of such a timely addition to the mental hygiene movement.

R. W. H.

Human Physiology. By PROFESSOR LUIGI LUCIANI. Translated by FRANCES A. WELBY. Price \$5.00. (London: Macmillan & Co., Limited, 1911.)

Luciani's *Physiology* stands midway between the text-book designed primarily for the use of beginning students and the reference book intended for those advanced in the subject. English readers will appreciate the charm of a new point of view in dealing with the problems of physiology—that of the Italian school, of which the author is an eminent representative. The book,

furthermore, brings to light a considerable amount of Italian work, which has suffered more or less oblivion because American readers, at least, have been prone to confine themselves to French and German sources. Perhaps the greatest charm, however, lies in the historical treatment of the subjects under discussion; here the author seems not only to have found delight himself, but to have been able to convey to the reader an equal pleasure in the slow but patient unfolding of the various problems through scientific effort.

As may be inferred from the fact that each volume contains over 500 pages, the book treats of the subject matter in considerable detail; nevertheless, it has the advantage over most modern texts of this size compiled by multiple authorship that the style and point of view are throughout that of a single mind. None but a physiologist of the old school versed in all the branches of his subject could make such a contribution. Those of us who have felt the pressure of specialization may well pause to appreciate and admire a work of this nature.

Luciani is a confirmed neo-vitalist. Long before his text-book was written we may infer that he despaired of a solution of the phenomena of life according to the laws of chemistry and physics. Since, however, these offer our sole line of approach, it seems unfortunate to belittle the efficacy of our resources; the younger worker particularly, whose dreams sustain a determined purpose and in whom failure is still an inspiration, will rebel against this point of view. However true it may be that our instruments break and fail us of accomplishment, yet it does not necessarily follow that instrumentation is wholly impossible. Vitalism to the young man is an admission of failure, and as such is incompatible with the spirit of youth. Indeed, too many problems in science have been lifted out of the shadow of vitalism and advanced toward simplification to allow a final judgment. That the phenomena with which physiology concerns itself in time break the will to solve them with the means at hand is readily apparent, but in the matter of lymph-formation, for instance, it seems to the writer that the author far overstates the significance of vital processes. Yet, however much we may distrust the neo-vitalistic conception of life, it is very proper that we should beware of the satisfaction of words and phrases—and this Luciani makes clear and imperative.

The author has sought successfully to place at the disposal of the reader many of the methods, operative, chemical and technical, which have advanced physiological thought, by detailed description of the procedures. Although these descriptions are not intended to supplant the assistance to be had in modern hand-books, they serve the useful teaching purpose of visualizing the method at hand.

Available sources of detailed information as to these methods and the chief contributions in literature are grouped at the end of the several chapters under the several subjects discussed. To this list, the editors of the English edition, Dr. Camis and Dr. Holmes, have added a selected list of English-written papers, which serves the double purpose of extending the field of available literature and of bringing the subjects down to a later date. The latter is a point of no small importance, in view of the present-day rapid extension of the science, and bears upon the one fundamental criticism of a book of this kind. Below, in referring particularly to the several volumes, the approximate date to which the literature has been followed will be stated. The fact that books, and especially text-books, serve their purpose and disappear is well apparent to everyone. It follows, therefore, that for practical application Luciani's text-book presented in English has necessarily depreciated in value. Nevertheless, the work of a master mind in any subject does not suffer greatly by the passage of time, provided the passage of time is appreciated by the reader. The beginning student should meet a subject brought fully up to date. The more mature student, however, can benefit

from the older text, and to him the book under review will have a lasting value.

The English translation is to appear in five volumes, three of which are at hand. The first two of these follow the third, while the last three follow the fourth Italian edition.

The first volume deals with the circulation and respiration. It opens with an introduction and three introductory chapters dealing with the fundamental aspect of the biological problem, the purpose of which is to orient the reader, in preparation for the specific discussion and treatment which is to follow. Here we meet the first note of neo-vitalism which permeates the entire text. The subsequent chapters are notable for their wealth of illustration in the reproduction of graphic records, apparatus, diagrams and histological preparations, many of the latter being in colored plates. One is impressed by the insistence of the author in ascribing the discovery of the general circulation of the blood to Cesaipinus rather than to Harvey. The author's literature comes down to about 1905; hence the work of Barcroft and of Haldane, in opening up the subject of alveolar air and respiratory regulation, and the newer studies on the chemistry of the blood, do not come under discussion.

The second volume deals with internal secretion, digestion, excretion and the skin. The author is of the opinion, based largely on experiments conducted in his own laboratory in Rome, that the function of the thyro-parathyroid system is to neutralize a *materia peccans*; that in the absence of the glands auto-intoxication results, and that there is no evidence of a true internal secretion. The pituitary gland is, by implication, associated in its function with the same system, while the suprarenals, as is universally accepted, discharge into the blood-stream a substance essential to the normal metabolic processes. In the section on digestion Luciani definitely opposes the hormone theory of Bayliss and Starling, particularly in regard to the formation of pancreatic *secretin*. The literature in this volume, as in the first, is brought down to about 1905, with the result that the recent work again fails of treatment.

The third volume deals with the muscular and nervous systems. This volume appeals to the reviewer as the most attractive of the three. It is profusely illustrated and, what is perhaps of more moment, the treatment of the subject matter covers the literature to a recent date, although it is to be noted that the theories of the English school on the chemical processes in muscular contraction are not mentioned in the text. The translation follows the 1913 Italian edition and has, therefore, been made available to English readers with commendable promptness.

In conclusion, it is of interest to state that one or other of the earlier editions has been translated into French, German and Russian, a reliable indication that the work has been widely recognized as possessing true merit.

D. R. H.

Exercise in Education and Medicine. By R. TAIT MCKENZIE, B. A., M. D. Price \$4.00. (Philadelphia: W. B. Saunders Company, 1915.)

This new edition is bound to have as great success as its predecessor. Indeed, one has only to look through it to realize the immense amount of good, available material there is in the book, not only as regards exercise in health and in education, but also in medicine. The first part of the book is devoted to exercises in general with their classifications, and contains excellent descriptions of the different systems that are in vogue throughout the world. Exercise, as it should be carried out in colleges and universities, as well as in schools and playgrounds, is dealt with fully, and there is an interesting chapter on the physical education of the blind and deaf mute. As regards exercises in medicine, there are so many conditions in which they are of great value that they need not be mentioned here. Each one in turn is gone into most thoroughly in different chapters, and new chapters have been

added on respiratory gymnastics, and the treatment of viscerop-tosis and functional disorders of the nervous system. The plates throughout are good and add greatly to the interest of the work.

J. A. C.

Occupational Affections of the Skin. By R. PROSSER WHITE, M. D., Ed., M. R. C. S., London. Price \$2.00 net. (New York: Paul B. Hoeber, 1915.)

There are numerous contributions to this field of dermatologic literature, but it is always gratifying to read a treatise which correlates the facts and arranges them in a handy and attractive form.

Even if the subject-matter in this volume is not as comprehensive as might be desired, it certainly has been handled well. The index is complete and well arranged, and appropriate words are properly emphasized by being printed in heavy type, so that the reader can find his way very easily. The author quotes sources of information very freely—a splendid advantage for the student or prospective writer—although there is occasionally some apparent carelessness or some typographical error in the spelling of an author's name; for instance, Brock for Brocq, Kienboch for Kienböck.

A book of this type is always a welcome addition to the literature of diseases of the skin. It emphasizes particularly the fact that many of the diseases met with in practice have a definite cause. It should naturally be the object of every physician who is called upon to treat a disease of the skin to inquire minutely into any probable cause; and this cannot be done too painstakingly; for, after all, this must in great part be the basis or rationale for an intelligent therapy. Moreover, if one could add to this a knowledge of the pathologic process involved, the way to therapy would be very clear. A great many practitioners have yet to learn the lesson that in dealing with diseases of the skin prophylactic and palliative measures are factors in therapy upon which too much stress can hardly be laid.

A perusal of this little book almost naturally recalls these thoughts to one's mind. The volume should, therefore, claim a place on the shelves of all physicians as a genuine book of reference for many conditions of the skin, which at first might appear to baffle any attempts at treatment.

I. R. P.

Medical Lectures and Clinical Aphorisms. By SAMUEL JONES GEE, M. D. Cloth, \$2.00. (New York: Oxford University Press, 1916.)

This little volume of Dr. Samuel Gee will give the reader a great deal of pleasure. It is so full of ideas and shows most clearly Dr. Gee's splendid grasp of clinical medicine. The account of the conflict of the medical profession with smallpox forms a most interesting chapter.

His aphorisms are to the point in most instances and remind one very much of some of the sayings of the ancients, written many centuries ago, but with such revision as brings them up to date.

J. A. C.

The Backwash of War. By ELLEN N. LA MOTTE. Cloth, \$1.00. (New York and London: G. P. Putnam's Sons, 1916.)

This series of war sketches reveals much keenness of insight and a genuine literary gift, by which the wards of the army hospital and the daily life of the sick and wounded are pictured with unmistakable vividness and reality. We see, as with our own eyes, the dirty, disordered wards, the distressed patients, the insufficient heating and lighting and the lack of comforts, which no amount of good nursing can remedy. Some of the sketches are touching and pathetic in the extreme; others portray human nature at its worst—a sordid Belgian mother who reluctantly remains to see her son die, two or more physicians of loose moral-

ity, a priest "with a yellow beard" seeking forbidden fruit, drunken orderlies and the like. The general effect of the little book is to make one pessimistic and unhappy. It is a depressing contrast to the little sketch, "A Joy Ride," by the same writer in a recent number of the *Atlantic Monthly*. One is tempted to ask, *Cui bono?* Human nature has its high and low aspects. We are stimulated to attain higher levels by deeds of heroism and self-sacrifice; tales of brutalities and gross happenings, on the contrary, depress and lower the standards of thought and effort. Why stir up "the dirty sediment at the bottom of most souls"?

H. M. H.

Practical Physiological Chemistry. By PHILIP B. HAWK, M. S., PH. D., Professor of Physiological Chemistry and Toxicology in the Jefferson Medical College of Philadelphia. Fifth edition. Revised and enlarged. Cloth, \$2.50. (Philadelphia: P. Blakiston's Son & Co., 1916.)

The new edition is distinctly different from the earlier ones; the book has been enlarged, new chapters appearing on nucleic acids; gastric analysis, intestinal digestion, blood analysis and metabolism. Its character has also changed. Whereas formerly it was essentially a book for medical students and practising physicians, its scope has now been broadened so that it will be of considerable value to the clinical laboratory and research workers.

In tending, however, to become a compilation of the most satisfactory procedures and methods of analysis in physiological chemistry, the work has lost some of the author's style and taken on much of the character of an encyclopedia of methods. The more important methods have been emphasized by the author in heavy type. The book should prove very useful to all medical men.

H. L. H.

The Physiology of the Amino Acids. By FRANK P. UNDERHILL, PH. D., Professor of Pathological Chemistry, Yale University. Cloth, \$1.35. (New Haven: Yale University Press, 1916.)

At present there is no book or monograph which furnishes an adequate and up-to-date summary of the part played by amino acids in the physiological processes in the human organism. This has been a distinct detriment to those engaged in the practice of medicine, as well as to the scientist interested in problems of metabolism and nutrition. The literature on this subject contains so many difficult details and covers so many pages that it is an extremely arduous task for anyone to devote sufficient time and energy to cover it with any degree of thoroughness. Frank P. Underhill, Professor of Pathological Chemistry of Yale University, has attempted to supply this need in the present volume. In the preface he states: "It has been, therefore, the aim of the writer to gather in one place the results which have thus far been obtained in the field of the biochemistry of the amino acids, thus affording the busy practitioner and others, whose resources for consulting original communications are limited, an opportunity of gaining a knowledge of the present-day problem in this field of nutrition." In order to fulfill his task, the author describes in a concise and clear way the origin of amino acids from proteins, the metabolism of amino acids and proteins and the rôle which amino acids play in health and disease, as in growth, intestinal putrefaction, etc. The book, as stated, is supposed to be for the general practitioner. In consequence the discussion of the subject is not complete and references to the literature are not exhaustive. From the clinician's point of view the book is an admirable one for those who desire a résumé of the subject from the strictly physiological chemical side. The clinical application of chemistry of the amino acids, such as the D:N ratio in diabetes mellitus, intestinal putrefaction, acidosis, etc., has not been given its proper value. It is to be hoped that from this book there may eventually result two volumes of which science

and clinical medicine are much in need: first, a thorough study of the whole subject of protein metabolism with a complete bibliography; second, a volume such as the present one with the addition of an adequate discussion of the practical clinical application of these problems.

H. O. M.

A Laboratory Course in Serum Study. (Bacteriology, 208.) By HANS ZINSSER, J. G. HOPKINS and REUBEN OTTENBERG. (New York: The Macmillan Company, 1916.)

This little book, being a protocol of a laboratory course in serology given by the authors at the College of Physicians and Surgeons, Columbia University, New York, is not presented as a manual of technical methods or as a text-book of serology, but "describes only work actually done with the students." In most instances only one method of procedure is detailed, as, for instance, on page 18 where the technique for obtaining blood from the carotid artery of a guinea-pig is outlined, no mention being made of the convenient cardio-puncture which accomplishes the same results. In spite of this, however, by reason of the minute instructions in approved methods, it should be found useful by many who, without previous training in routine technique, wish to undertake the commoner forms of serological diagnosis. Pre-eminently the book will find its field of usefulness in the classroom, both to student and teacher; to the student because of its clearness and practicability, and to the teacher because of the detailed way in which the course is outlined throughout and adapted to the conditions of the class-room.

The course as outlined is calculated not only to teach the elements of serology in an attractive way, but also to train students in experimental methods. As such it is to be highly commended. The authors have made practical use of a demonstration in immunity by including as part of the course the immunization of the students against typhoid.

On the whole this book maintains the standard of excellence the profession has learned to expect from this laboratory.

F. A. E.

Practical Points in the Diagnosis and Treatment of Heart Disease. By E. M. BROCKBANK, M. D. Second edition. Cloth, \$1.25. (New York: Paul B. Hoeber, 1916.)

With the exception of the parts dealing with the heart sounds and murmurs, clearness has been sacrificed to brevity.

There is no mention of lues in relation to lesions of the aortic valve nor of the removal of focal infections under treatment. There is also no mention of the associated physical signs to help in the differentiation of the murmurs. The book is well bound and well printed.

D. W. C., JR.

The Art of Anæsthesia. By PALUEL J. FLAGG, M. D. Cloth, \$3.50. (Philadelphia: J. B. Lippincott Company, 1916.)

The book contains much practical matter which should prove of interest to the student of anæsthesia. It sets forth in a simple and expressive form the essential laws of anæsthesia drawn from the wide personal experience of the author. In its clearness and simplicity it is most convincing. If Dr. Flagg's teachings were taken to heart by beginners in the art, the effect for good would surely be felt.

Burdett's Hospitals and Charities, 1916. Being the Year Book of Philanthropy and the Hospital Annual. Containing a review of the position and requirements, revenue and cost of the charities. An exhaustive record of hospital work for the year, etc. Twenty-seventh year. By SIR HENRY BURDETT, K. C. B., K. C. V. O. Author of "Hospitals and Asylums of the World," etc. (London: The Scientific Press, Limited.)

As will be seen by the title, Burdett's review for 1916 has now reached its twenty-seventh year. The appearance of the present volume has been much delayed by hindrances incident to the war,

such as the difficulty in securing data for the reports and the increased cost of production consequent upon the scarcity of labor and the higher price of paper. The usual carefully analyzed statistics are given, but it is noticeable that the hospitals themselves have not cooperated to the same extent as formerly. The statistics are for the year 1914.

The author tells in glowing terms of the marvelous effect of the great war upon voluntary hospitals and also upon the methods of individual workers, and of the great improvement which has come about in the administration of hospitals, by which they have been changed from civil to military organizations. He also speaks of the improved morale of the hospitals as the result of the extraordinary cheerfulness, endurance and patience shown by soldier patients, who seem to have been grateful and appreciative for all done for them. It is interesting to note that the presence of these soldiers has produced increased revenues because of personal appeals for aid. There have been many changes in the staffs of the hospitals by reason of the fact that physicians have gone to the front to take care of sick and wounded soldiers. There has been a great increase in the number of hospital beds. It seems almost incredible that this increase should have amounted to 100,000 beds.

We regret to see that the editor feels that his excellent and useful work has not been duly appreciated in England because the thorough discussions of general hospital matters have not produced abundant fruit in increasing legacies to the hospitals. He also feels keenly the fact that the book has not been properly noticed by the newspapers. It would seem, however, that while the book may not make a popular appeal or furnish such material as newspapers desire for startling and sensational head-lines, it none the less has a fixed place in the public mind as a careful, painstaking and authoritative review of all which pertains to hospital work year by year.

The present volume speaks of post-graduate medical teaching, of training school facilities in poor-law infirmaries, and contains a list of territorial hospitals. The chapters are interesting but brief.

We regret to see an intimation on the part of the accomplished editor that he anticipates relinquishing his editorial work. He laments that the position which he is to vacate when he arrives at the age of three score years and ten has not yet been filled. It is to be hoped that the same guiding hand that has presided over the book during the past 27 years may still look after it for an indefinite future.

H. M. H.

The Treatment of Diabetes Mellitus, with Observations upon the Disease. Based upon 1000 Cases. By ELLIOTT P. JOSLIN, M. D., Assistant Professor of Medicine, Harvard Medical School, etc. Cloth, \$4.50. (Philadelphia: Lea & Febiger, 1916.)

Recent improvements in the treatment of diabetes—mainly through the introduction of fasting and the emphasis on the value of physical exercise by Dr. Allen—have created a demand and need for an up-to-date text-book on the treatment of diabetes. A wide and successful experience in treating diabetes, a keen appreciation of the value of physiology and laboratory methods in this disease, and an admirable ability to systematize, combine to make Dr. Joslin an almost ideal author for such a book.

Section I of the book begins with the author's distinct definition of diabetes mellitus, and consists in the main of statistics, gathered largely from his own cases. Especially interesting is the résumé of the factor of heredity and the unique method of discussing the etiology of diabetes. Section II treats of the pathological physiology of the diabetic, including a long discussion of acidosis. Section III is entitled "The Examination of the Urine, Blood and Respiration," and consists largely of descriptions of well-chosen methods. Section IV contains a discussion of the

dietetics of the diabetic—the energy, carbohydrate, fat and protein requirements and the availability of various foods for meeting these needs. Section V takes up the treatment; one finds here the simple scheme which he had previously published, augmented by the description of cases illustrating the “sources of danger.” The problems of impending coma, of surgery, of pregnancy in diabetes are fully discussed. The author is a firm believer in educating his patient; thus, in Section VI, there is a “primer” on “What every diabetic should know.” Other helpful points in the practical management of cases, as sample diets, charts and food tables, are included in the last two sections.

Very few faults can be found in the book; possibly the tables on food values might better have been less scattered; the frontispiece seems rather unfortunately overemphasized. But the virtues of the book completely hide its faults. It is admirably written, the explanations are simple and well presented. The book should claim a prominent place in the library of every practitioner.

H. L. H.

Diseases of the Skin. By RICHARD L. SUTTON, Professor of Diseases of the Skin, University of Kansas School of Medicine. (St. Louis: C. V. Mosby Company, 1916.)

A book by one who has had such a wide experience in dermatological fields as Dr. Sutton and who has been such a constant contributor to dermatological literature cannot fail to arouse considerable interest when it first appears for public inspection.

The text has 916 pages, with 693 illustrations and 8 colored plates. It presents in a conservative manner such new lines of treatment as the “autogenous serum injections,” and incorporates recent investigations such as Rosenow’s work on Herpes Zoster and that of Clough on foot and mouth disease in man.

The author is to be especially congratulated on the large number of excellent photographs that illustrate the book. The various types and modifications of most of the diseases of the skin are well represented in a carefully selected series. The pathology is fully discussed, and there are a number of very good microphotographs.

Somewhat iconoclastic ideas are advanced in the discussion of eczema, the refuge of the general practitioner and often of the specialist, when it is referred to as “a sort of dermatological scrap-heap”; however, most of us must acknowledge that our conception of this disease is often very diffuse and indefinite.

Dr. Sutton’s book, on the whole, is clear, the subjects being presented in an easily digested form. It is up to date, but not loaded down with a lot of obsolete literature, and the illustrations are numerous and excellent. It can be highly recommended to anyone seeking dermatological knowledge, whether it be the student hunting fundamental facts or the specialist attempting to place some of the rare skin manifestations.

L. W. K.

Surgical and Gynecological Nursing. By EDWARD MASON PARKER, M. D., F. A. C. S., and SCOTT DUDLEY BRECKENRIDGE, M. D., F. A. C. S. 134 illustrations. Cloth, \$2.50 (Philadelphia and London: J. B. Lippincott Company, 1916.)

This work is a worthy contribution to the many small volumes published for the use of nurses. Its contents are limited to the care of surgical and gynecological patients, and it contains sensible material and practical suggestions for the care of these cases. The chapters dealing with the comfort of the patient and post-operative complications are valuable, and the descriptions of the various methods of bandaging are complete. Fewer pictures of the sterilizers would have sufficed and the space might have been utilized for illustrations of methods for giving treatments, such as bladder catheterization and irrigation, vaginal douches and the proper care of the infusion apparatus and the breast area during hypodermoclysis.

Medical students in the last two years of the course can also read the book with profit.

C. W. V.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pædiatrics, Obstetrics, Gynecology, Orthopædics, Pathology, Dermatology, Ophthalmology, Otology, Rhinology, Laryngology, Hygiene, and other Topics of Interest to Students and Practitioners. By leading members of the medical profession throughout the world. Edited by H. R. M. LANDIS, M. D., Philadelphia, with the collaboration of ten additional editors. Vols. 1 and 2, 26th series, 1916. (Philadelphia and London: J. P. Lippincott Company.)

As might have been expected from those that have gone before, these two volumes contain many excellent articles, although of unequal scope and varying importance. Among the more important may be mentioned Friedenwald’s “Early Diagnosis of Gastric Cancer”; Young’s “Tetanus: Lessons Gleaned from the War, Modern Research and Private Practice”; Robinson’s “Auricular Fibrillation: The Cause and Its Relation to Ventricular Activity”; Bowers’ “The Relation of Mental Defect to Crime”; Martin’s “Colon Resection and Its Indications,” and Osgood’s “Orthopædic Problems Presented by the European War.” It is much to be regretted that space will not permit more than an enumeration of the titles of these papers. The volumes are worthy of thorough study.

H. M. H.

Christianity and Sex Problems. By HUGH NORTHCOTE, M. D. Second edition. Revised and enlarged. Cloth, \$3.00. (Philadelphia: F. A. Davis Company, 1916.)

This work is modestly stated by the author to be written with the expectation that after a few years it might be found to be “quietly useful.” It is written as a study of a difficult subject and not as a polemic, to advance a theory or to support a cause. It contains a careful statement of the problems of sex and gives the teachings of the Bible and of the teachers of the church bearing upon them. There seems a little tendency to rely too much upon authority and too little upon reason in the final settlement of some of the problems. The complexity of the problems involved forbids any critical consideration of them in the present review. The fair-mindedness and sincerity of the author win confidence. The book is in marked contrast to the usual treatises upon sex matters, and can be commended to the careful reading of all persons who are honestly in search of guidance.

H. M. H.

Sexual Impotence. By VICTOR G. VICKE, M. D., Consulting Surgeon to Mount Zion Hospital, San Francisco. Fifth edition. Enlarged. Cloth, \$2.25. (Philadelphia and London: W. B. Saunders Company, 1915.)

The appearance of a new edition of this work after a period of three years indicates a steady demand for the book. The additions to the last edition are largely in the direction of treatment. The author has very sensible ideas upon psychotherapy and is much encouraged by his experience with psychoanalysis. The whole book is judicious and characterized by moderation and good common sense.

H. M. H.

Clinical Disorders of the Heart Beat. By THOMAS LEWIS. Third edition. Cloth, \$2.00. (New York City: Paul B. Hoeber, 1916.)

That the second edition of Dr. Lewis’ book should have been exhausted in two years speaks for its popularity with the medical profession. The subject-matter is presented in the same order as in the former edition. Minor changes have been made in words here and there throughout the text. In the chapter on heart block reference is made to adrenalin in the treatment of the “fit,” but the author merely states that it has been suggested. In the treatment of the “Abrupt onset of partial heart block”

full exposure to the open air, the author thinks, "deserves a thorough trial."

The insertion in the chapter on auricular fibrillation of the influence of this condition on thrombosis and infarction is an addition to the work.

More extended observation seems to have shown the greater frequency of "alternation of the heart" in general hospital patients than was given in the last edition.

Throughout the present work the illustrations and figures of the former edition have been retained with their explanations.

The book presents the subject clearly and concisely and is too well known to require a more extended review.

H. R. C., JR.

The Treatment of Acute Infectious Diseases. By FRANK SHERMAN MEARA, M. D., PH. D., Professor of Therapeutics in the Cornell University Medical College in New York City. (New York: The Macmillan Company, 1916.)

The purpose of this volume on "Treatment of Acute Infectious Diseases" is to present its material in a thoroughly practical and useful way. The author discusses the therapy of the acute infections in a fascinating manner. He drives home his ideas in ringing sentences that leave no doubt in the reader's mind as to his exact meaning. Such episodes in the thread of thought as the following are not uncommon: "The contrast between a well-ordered, neat, cool sick-room, and a hot, stuffy room, with six or ten visitors, gas jets in full action and babel and chaos regnant, is one of the most striking that can be witnessed." Experimental and scientific observations are quoted as far as possible to furnish a reasonable basis for each therapeutic procedure. Of course, however, many of these still rest on clinical empiricism, and it is in this connection that Professor Meara's wide experience and his keen judgment give the constant use of the personal pronoun, "I am convinced" and "I believe," a significance that cannot be underestimated. The presentation of the subject is complete, thorough and very lucid. By means of subheadings attention is called to bed, room, diet, drugs, specific treatment, etc., in each disease. Furthermore, there is a very well-arranged and suggestive summary at the end of each chapter. The book is complete to the minutest detail in its therapeutic directions; it is written in a very lucid style, so that the subject-matter can be quickly assimilated without any doubt on the reader's part of the author's meaning, and finally, the judgment exhibited in the principles of treatment advocated is excellent.

H. O. M.

Gynecology. By WILLIAM P. GRAVES, M. D., F. A. C. S., Professor of Gynecology at Harvard Medical School. 8°. 770 pp. 424 original illustrations; 66 in colors. Cloth, \$7.00 net; half morocco, \$8.50 net. (Philadelphia and London: W. B. Saunders Company, 1916.)

New ideas and an attractive arrangement of the material characterize this recent addition to the works on gynecology. The subject is divided into three parts, dealing respectively with the physiology and relationship of gynecology to the general organism, gynecological diseases and operative gynecology. One important contribution, thoroughly treated in the first section, and mentioned throughout the volume in connection with various conditions, is the consideration of the glands of internal secretion. This field of medicine now being extensively studied, and heretofore omitted from works on gynecology, is dealt with in a practical way; and this portion adds much to the completeness of the work.

A full list of the gynecological diseases is included in the second part and the descriptions here given, although in many

instances brief, are accurate and clearly set forth. In the operative section the usual gynecological operations are described, and many are accompanied with illustrations, more or less diagrammatic. In a work of this size one would expect more consideration to be given to the pathological conditions of the urinary system and their treatment, and this lack materially detracts from the book's sphere of usefulness. Extra-uterine pregnancy and dysmenorrhea are well treated, but no mention is made of the subject of threatened or incomplete abortion.

The volume is fully illustrated with microscopic drawings and illustrations. The latter, which are by the author, are creditable productions and readily convey the idea intended. Those on pages 522 and 523, however, are misleading and should be improved.

In brief, the work is well written; it contains the important parts of gynecology concisely stated and attractively presented. It will be of decided value to both students and practitioners.

C. W. V.

Home Care of Consumptives. By ROY L. FRENCH. 12°. 200 pp. Cloth, \$1.00. (New York: G. P. Putnam's Sons, 1916.)

The author is a social worker who has been actively identified with tuberculosis work for several years and has even had the disease in his own family.

For patients discharged from sanatoria the book reiterates principles laid down in the institution and emphasizes the need for lifelong care and watchfulness. For patients without the advantage of sanitarium instruction it deals in a definite, practical way with questions of home nursing without expensive equipment, with the social aspects of the disease and the relation of patient to physician. Without unwarranted optimism it offers substantial encouragement to the patient and his family. Dispensary physicians will find in it many useful suggestions.

M. A. H.

Nerves. By DAVID FRASER HARRIS. University Library of Modern Knowledge. (New York: Henry Holt & Co., 1916.)

This little octavo volume contains 10 chapters together with a glossary, useful for the layman or student, and an index. In his preface the author says: "The following pages . . . attempt to explain in non-technical language the place and powers of the nervous system." And later: "It is hoped that those whose previous knowledge of physiology and psychology is small may learn something of the way in which this complicated system does its work; and that those who happen to know something of these subjects may yet gain more from an account of innervation which is as accurate as popular terminology allows it to be." The book is at once readable and instructive, and anyone of either category of readers who takes it up will read it through. At all times, science tempered by sound common sense can hardly fail to be attractive; and this book contains both.

F. R. S.

Gould's Practitioner's Medical Dictionary. Third edition. Revised and edited by R. J. E. SCOTT, M. A., B. C. L., M. D., of New York. XX + 962 pages. Flexible cloth, round corners, marbled edges, \$2.75. (Philadelphia: P. Blakiston's Son & Co., 1916.)

The compactness, clearness of type and convenient form of this admirable dictionary commend it to every general practitioner. It includes all current words and terms and gives concise and clear definitions with the correct pronunciation of each. In the present edition 20,000 new words have been added, and the volume of about 1000 pages contains upwards of 70,000 words in the aggregate. It is worthy of high praise.

H. M. H.

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Physiology
H.H.L.

BULLETIN

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THE RECENT EPIDEMIC OF INFANTILE PARALYSIS.¹

By DR. HAVEN EMERSON, New York City.

Since the early summer of 1916 there have been 24,000 cases of infantile paralysis in the United States. Eighteen thousand of these were in New York City and the adjacent territory, in the States of New York, New Jersey, Pennsylvania, Connecticut and Massachusetts, the Borough of Brooklyn being the first to become infected. As an instance of how the infection was spread, I may mention the experiences of three Brooklyn families with 10 children, whose mothers took them each day to Prospect Park to be out of doors. On the 30th of June one child had an acute attack of fever. The family practitioner was called in and prescribed a laxative, light diet and rest in bed for a few days. The child was kept in bed and four days later the mother noticed that he was not able to get up and stand upon his feet. Further rest was prescribed, and at the end of a week the child was able to get up and the case ran on to gradual recovery. Seven days after the onset of the sickness in the first child, one of the other children developed an acute form of fever and weakness of one leg, which was so obvious that the mothers became frightened and took all of the children out of the state into Wayne County, Pennsylvania. Forty-eight hours after arrival the rest of the children came down with the disease and two died. From such examples as this, we should

consider that we were dealing with a pretty readily communicable disease, and yet there were many instances in which the disease appeared to be not epidemic in type at all. For instance, in one institution full of children, one case was not followed by any secondary cases.

The distribution was independent of sanitary conditions. There were no cases on Governor's Island, the Federal military station in the harbor of New York. There were 87 children on that island, which was quarantined most effectively at the beginning of the epidemic. Barren Island, situated in Jamaica Bay, is a place to which all the city garbage is brought by boat. All the city's dead animals, often two or three thousand a day, are brought there; it has no public water supply, no sewerage system, the houses have no cellars, no garbage collection, and the people have few garbage cans, the household waste being thrown on the ground about the shanties. There are 1700 people on the island, 350 of them being children, but there was no case of poliomyelitis on that island all summer. Smells, flies and insanitary conditions have prevailed, but because of its geographical position and the social condition of its people, the island is more or less isolated. Where the congestion was least in the city, in the Boroughs of Queens and Richmond, there the cases were most frequent, in proportion to the population.

¹ Read before a meeting of The Johns Hopkins Medical Society, November 6, 1916.

The most constant symptom was found to be the acute onset of fever. The symptom one would think of next in seeing these children would be the change in the character of the child. It becomes more than usually irritable and is unwilling to be fondled and held. If you will analyze that, you will realize that this is the only disease we know of in which the child does not want to be picked up by its mother. In other words, it does not want to be picked up and have its spine flexed anteriorly. It exhibits the so-called spinal sign on flexion.

I feel that we should get along a great deal faster in our general knowledge of this disease if we abandoned the use of the word "abortive." We are dealing with a disease which has paralysis, or which exists without it. It is not uncommon to have a rise of temperature seven days after the onset of the disease, with a sudden development of a paralysis which has not previously existed. These cases were in children admitted to hospitals in the pre-paralytic stage of the disease. We have got the habit of using the terms pre-paralytic, non-paralytic and paralytic. There were many children found with the typical symptoms who never developed a paralysis. I feel that we have no right to consider these as abortive forms of the disease. When those children were examined, they showed all the evidences of a general infection, but it did not go on to a paralysis. To call a case abortive simply because there is no paralysis is apt to cause the physician to feel that he has a patient who is no longer in danger. We must consider that a diagnosis is as important in the absence of paralysis as with paralysis, and the patient an equal, if not a greater danger, as a distributor of the virus.

The experience of our laboratory technicians was that we rarely found a fluid that was not clear, when lumbar puncture was done. If one holds this apparently clear fluid up in the sunlight, the little sparkles that disclose the presence of the cells can be seen, but it looks like clear fluid. In our experience, the fluid was rarely turbid. Under high pressure, with a cell count rising and falling pretty abruptly, one may get the fluid before there is a noticeable increase in the cell count and before the globulin has become noticeable. Again, in a case which has had a doubtful course, one may get the spinal fluid after the time when the cell content has increased, and there may only be the globulin as a guide. The cell count varies considerably, and yet a clear fluid, with an appreciable increase in cell count and globulin has been considered characteristic and diagnostic, when found in a child with the symptoms of an acute febrile infection, even in the absence of any paralysis.

The mortality in this epidemic was much higher than formerly quoted. In the city as a whole the case fatality was 26.96%. In the Borough of Richmond, 19.93%; in the Borough of Queens, 27.99%; in Brooklyn, 21.60%; in the Bronx, 25%; in Manhattan, 28.43%; in Nassau County, L. I., 24%. In the State of New York as a whole, and not including the city, it was 21%, a uniformly higher case fatality than in previous epidemics.

The preventive measures suggested were similar to those given in Osler, the additional advice being given that children

should avoid eating uncooked fruit throughout the summer, not because we had any knowledge of danger in uncooked food, but because of the knowledge that most diseases that are carried from person to person may be spread in this way. In order to be quite fair about the milk supply, we took all the cases in Richmond and the Bronx and studied each one as we would have done in the beginning of a typhoid epidemic. No clues indicating that the milk had any influence on the origin or spread of poliomyelitis were found.

There were 4500 cases in the Department hospitals. From the observations which I had a chance to make in the hospitals and from the reports of the physicians in charge, it was evident that no single therapeutic agent proved so useful in giving prompt relief as lumbar puncture. Before there was any general use of adrenalin or the use of normal serum, many cases were treated in our hospitals simply by the withdrawal of spinal fluid, which was often followed by brilliant results. It is only fair to add that there were cases which showed prompt recoveries from severe attacks without any withdrawal of fluid or any other than expectant treatment. Children beginning to develop contractures, and children so uncomfortable they could not sleep, were much helped by warm baths and warm wrappings about their arms and legs. The longer the cases remained in the hospitals and the more the neurologists and orthopedic surgeons studied them, the longer did they postpone any attempt at interference by massage, electricity, or mechanical contrivances on the affected muscles of extremities. The muscles are essentially fatigued and must be rested a long time. It is obvious that many muscles apparently able to take care of themselves are really trying to meet the pull of the strong group on the other side of the lever, which have not been paralyzed.

During the quarantine period, which we have established in New York as eight weeks, the muscles rarely need manipulation of any kind. The opinion has become stronger and stronger throughout the city that premature interference has done more harm than good in the past.

A specific serum has been shown to exist, but that that serum is a curative agent of constant value is quite a different matter. We have had 350 cases treated with the serum of recovered cases, and the results are now being carefully studied.

In the following figures we used the case rate per thousand instead of per hundred for our results:

Borough.	Population.	Poliomyelitis Case Rate Per 1000 Population.
Manhattan	2,634,000	.94
Bronx	575,000	1.16
Brooklyn	1,928,000	2.24
Queens	366,000	3.22
Richmond	97,000	2.92

The most sparsely settled boroughs had rates a little over three times as high as the rate in the Borough of Manhattan and the Borough of Brooklyn, with its tremendous number of cases, had a case rate less than the boroughs of either Richmond or Queens. I have already mentioned the death rate, which shows that the disease took one out of every four patients.

The question comes as to the number of patients we got.

Did we get a complete notification of the disease? This is best answered by a chart prepared by the Department, which shows the number of cases reported and the number we afterwards found to have existed at that time. For instance, on the 8th of June the report came in that a number of babies had been found at the Health Station with paralysis of the arms or legs. These were all in the little district of Brooklyn, the shore front of the Atlantic basin, where the disease started. On the 22d we found three cases reported and later we found there were 26 cases of the disease on that day. That is the margin of error in public health administration. On June 22 we enlisted the help of the lay press and told the people we wanted all the cases of paralysis reported. From that time on there was a general understanding among the public that there was a lot of the disease and people began to do that which is desired by all health officials, *i. e.*, report more cases than there were. When people begin to report cases on suspicion, then you begin to be at the point of controlling the situation. On the 3d of August 239 cases had their onsets, and these cases reached our hospitals 48 hours after the onset of the disease, which is about as close as a department can get to having a case verified and under proper control after onset.

We were of course interested in all sorts of possibilities as to the cause of the epidemic. We thought perhaps the heat might have something to do with the situation, and also the humidity. The only thing we could work out was that the deaths are pretty apt to come coincidentally with the height of the humidity, which would be the case with almost any acute infectious disease in little children under five years of age. When one realizes that the deaths are mostly respiratory and that the children are in many instances from poor homes (although the majority did not appear to be in poor condition) the relationship between the humidity and the deaths is pretty obvious. We got little or nothing positive out of these observations on the relation between onset and deaths, and temperature or humidity.

The crude death-rate for the entire city will be only a point or two higher than that of last year. All other infectious diseases have been consistently lower than at any other time in the past five years, for the reason that all parents this summer have taken a great deal more trouble about their children than usual. There have been also a great many things children were spared because the parents were afraid to take any chances this year, in the face of the constant daily advice given by physicians, nurses and others.

Every case of death reported as due to poliomyelitis was followed by a careful investigation, and the descriptions were so simple you could not mistake them. The patients died of failure of respiration in practically all cases (98%). A number died after a prolonged period of unconsciousness and exhaustion, going through what one sees in tuberculous meningitis.

At present, out of every hundred cases reported to us, we are willing to accept as true cases about forty. Out of all the cases we have accepted, 15% showed no paralysis at any time,

18% more showed no paralysis at the end of eight weeks in the hospital, and the rest of them showed paralysis persisting at least until after they had left the hospital. All cases that did not have obvious signs and perfectly clear clinical pictures on admission were kept isolated until the diagnosis was arrived at, and in no instance, in which patients were found on examination to be free from poliomyelitis, did they develop the disease as the result of exposure in the hospital. Further, no doctor and no nurse, either in the field service or in the hospital service, developed this disease during the entire time of the epidemic in New York.

A group that offered an interesting study was that of the children in the institutions in the city. I may say that these institutions in New York City are under the observation of the Department of Health. There are 93 institutions where children are cared for permanently, containing 21,746 inmates; 76 more institutions take children in temporarily, such as day nurseries and summer camps. These take care of 6365 more children, making a total of about 28,000. Among these institutions there were two cases that were properly attributable to conditions in the institutions after quarantine had been established. At the beginning of the epidemic warning had been sent to all these institutions to close their doors against visitors, and that quarantine should be enforced for three weeks for new admissions, before allowing them to mingle with the rest of the children. In St. Joseph's Home, one child developed the disease on the 8th of August simultaneously with the child of the engineer of the institution, who lived outside of the grounds, his house, however, abutting the buildings of the institution, and who had been in the habit of bringing in his child in its carriage each day and keeping it in the garden near the power-house. We had no clue to the person who infected these two children, but as the engineer was a worker in the institution and lived in the house where the other case developed, we suspected he must have played a part. In an institution of 98 children at Huguenot, which was quarantined on July 4, one child developed the disease on August 23. He was unconscious from the time of onset, and remained so for 10 weeks until he died. We did not get an autopsy and the spinal fluid was not characteristic. Nobody could confirm the diagnosis clinically, and yet in the absence of other proof, we must accept this on our list as a case of poliomyelitis. There was a possibility in this case of tuberculous meningitis and also of acute hydrocephalus, but proof was lacking. There are also other clinical possibilities. The unconsciousness with wasting, no sharply localized paralysis and no other confirmatory signs make us suspect that this was not a case of poliomyelitis. We should feel that the isolation of children and the manner of living in the institutions was disadvantageous for the spread of the disease.

The best summary of the whole situation is the report prepared with the approval of the Public Health Association, which met at Cincinnati last week, and which will shortly appear in some of the medical journals. The report is as follows:

The Committee of the American Public Health Association, appointed by the President to report upon the subject of poliomyelitis, begs to submit the following:

The specific cause of poliomyelitis is a microorganism, a so-called *virus*, which may be positively identified at present only by its production of poliomyelitis in monkeys experimentally inoculated. Such experiments have shown this virus to be present not only in the nervous tissues and certain other organs of persons who have died of poliomyelitis, but also in the nose, mouth and bowel discharges of patients suffering from the disease. It has been proved by similar experiments that healthy associates of poliomyelitis cases may harbor the virus in their noses and throats.

These experiments, together with the fact that monkeys have been infected by direct application of the virus to the mucous membrane of the nose and by feeding of the virus, are strong evidence that in nature infection may be directly spread from person to person.

Observations on the occurrence of the disease might seem at first thought to be inconsistent with this conception, since contact between recognized cases can seldom be traced. However, this may be adequately explained by the lack of means for detecting mild non-paralytic cases, and by the belief that healthy carriers of the virus and undetected cases are considerably more numerous than frankly paralyzed cases.

Many facts, such as the seasonal incidence and rural prevalence of the disease, have seemed to indicate that some insect or animal host, as yet unrecognized, may be a necessary factor in the spread of poliomyelitis, but specific evidence to this effect is lacking, and the weight of present opinion inclines to the view that poliomyelitis is exclusively a human disease and is spread by personal contact, whatever other causes may be found to contribute to its spread. In personal contact we mean to include all the usual opportunities, direct or indirect, immediate or intermediate, for the transference of body discharges from person to person, having in mind as a possibility that the infection may occur through contaminated food.

The incubation period has not been definitely established in human beings. The information at hand indicates that it is less than two weeks, and probably in the great majority of cases, between three and eight days.

If the foregoing conception of the disease is correct, it is obvious that effective preventive measures approaching complete control are impracticable, because isolation of recognized cases of the disease and restraint upon their immediate associates must fail to prevent the spread of infection by unrecognized cases of carriers.

These difficulties would appear to be inherent in the nature of the disease. Nevertheless, we may hope for the development of more thorough knowledge which will permit of more effective control of the disease than is now practicable. Of first importance is the more general recognition by practitioners of non-paralytic cases through clinical observation and laboratory procedures.

Lumbar puncture has been shown to offer valuable aid in diagnosis, and a more general use of this test is to be encouraged, since it not only facilitates accurate and early diagnosis,

but in many cases affords symptomatic relief as a therapeutic procedure. Without undertaking to predict the future progress of research, we may hope for certain possible developments which may afford far more effective control of the disease, with substantial relief from many inconveniences at present inevitable. Among those possibilities we would include: A practical test for the detection of all clinical types and carriers; a simple and reliable test for distinguishing between susceptible and insusceptible persons; and means of conferring artificial immunity against poliomyelitis.

At present our information demands the employment of the following administrative procedures in attempting to control the disease:

1. The requirement that all recognized and suspected cases be promptly reported.
2. Isolation of patients in screened premises. The duration of infectivity being unknown, the period of isolation must necessarily be arbitrary. Six weeks has been recommended by the Conference of State and Territorial Health Officers with the Surgeon-General of the Public Health Service as sufficient, and this period has been generally accepted throughout the United States.
3. Disinfection of all body discharges.
4. Restriction of the movements of intimate associates of the patient so far as practicable. This should include at least exclusion of the children of the family from schools and other gatherings.
5. Protection of children so far as possible from contact with other children or with the general public during epidemics.
6. Observations of contacts for two weeks after the last exposure.

There is no specific treatment of established value in poliomyelitis. During the persistence of the acute symptoms of the disease, the important principles of treatment are rest in bed, symptomatic relief, and passive support for the prevention of deformities. Active measures during this stage are not only useless but are apt to cause serious and often permanent injury. Hospitalization of patients where possible is to be encouraged. The best chances of recovery from residual paralysis demand skillful after-care, often long continued, and always under the direction of a physician familiar with the neurological and orthopedic principles of treatment. The provision of such after-care often becomes a community problem, demanding the cooperation of all available agencies, social and professional.

DISCUSSION.

DR. JANEWAY: After the amount of food for thought that Dr. Emerson has provided us with, it is scarcely fitting for any of us to add our small crumbs to the hearty meal. One thing I would like to add, however, and that is a word of appreciation to Dr. Emerson from an old colleague of his in the Department of Medicine at Columbia for his magnificent work during this past summer. Dr. Emerson started as a physiologist, then came over to us and became a medical man and acquired his interest in public health only somewhat later in his career. Perhaps his medical training has not been without its value to all of us in his recent position in control of this epidemic, because among the things the epidemic will give in the future will be a study of the clinical side

of poliomyelitis on a scale absolutely unparalleled hitherto, largely due to the segregation of such large numbers of cases in the hospitals and to his prompt recognition of the importance of the diagnostic problem in any attempt at control. From the early days of the New York epidemic the diagnosis was in the hands of an extraordinarily competent group of men, all very specially trained in the recognition of the disease. Many facts of clinical importance will unquestionably come out later in their reports.

There are one or two questions I should like Dr. Emerson to answer from his experience if he can. The question of second attacks is one in which I have been much interested. Dr. Holt told me a couple of weeks ago of a fairly conclusive instance of a second attack in a child who had been affected some years previously.

Dr. Emerson did not bring out on the epidemiological side the relation the opening of schools, a point of immediate interest to us in Baltimore, had to the subsidence of the epidemic.

One very striking feature, which anyone who knows New York institutions will recognize, is the extreme difference between this disease and such a one as measles. His report of the existence of only five cases of poliomyelitis in the Foundling Hospital, without the decimation which would always have occurred in an institution of that type if such a disease as measles started. This is one of the problems of the transfer of poliomyelitis by personal contact. That experience seems to me of great importance in determining eventually, as I hope Dr. Emerson will be able to determine, the efficacy of such methods of quarantine as have been adopted in the epidemic during the past summer.

If Dr. Emerson has any time at the end, I should be glad if he could say a little more as to the types of non-paralytic cases, bearing on the question of the possibility of the recognition of these cases. We stand between Scylla and Charybdis. In the presence of an epidemic we are likely to call everything that bears the slightest resemblance to poliomyelitis a proved or almost proved case; and in the absence of an epidemic we are almost certain to fail to recognize cases which are perfectly definite examples of the disease. I am interested especially to know whether definite clinical evidence of meningeal irritation was to be found in almost all of the early cases.

DR. JOHN D. BLAKE, Health Commissioner, Baltimore: The first case of poliomyelitis in Baltimore was reported on July 26. On the 28th of July there was a second case, which came in from Philadelphia. We then went to the mayor for an appropriation for a hospital for these cases, so that there might not be scattered foci throughout the city. As soon as a case was reported it was taken to the hospital. We had but two cases in July, but on the first of August the disease began to increase. We then got in touch with the State Department and insisted on a quarantine. About that time Dr. Ford came back to Baltimore and was of great assistance in establishing the quarantine, which was instituted against New York, Pennsylvania and New Jersey. This was carried out with great difficulty, as people would arrive from outside the state with suspicious cases and the railroads would not take them back, and we had to take care of them until they could be sent home. We also instituted an order that all cases dying should have an autopsy, and no case was decided to be poliomyelitis until it had been so diagnosed by our diagnosticians. There were 186 cases in the city, and there have been 60 deaths to date, a mortality of 34%; 138 of the patients were white and 48 colored. We had 75 white cases before we had one colored, which led us to suspect at first that perhaps the colored race was more or less immune. Six cases were treated at home, where first-class quarantine could be obtained. The results in Baltimore seemed to indicate an infection by contact.

DR. JOHN S. FULTON: The clinical side is so interesting, I hesitate to speak as a public health man. During the second or third weeks in August I imagine the position of Health Commissioner

of New York City must have been as unenviable a one as any public health man in this country could have had. A little later there was a public health conference, held in Washington with the Surgeon-General of all the public health authorities in the United States, to which Dr. Emerson was invited. He was good enough to accept the invitation. At that time Dr. Emerson was not personally known to the health officers of all the states of the United States. What he did by appearing at that meeting was to make himself known to these officers and to inspire in them the utmost confidence. That conference was one of the symptoms of the psychosis occurring in consequence of the New York epidemic and Dr. Emerson did very much to settle it and make a beginning of its end.

In Maryland we had had no idea of what it would mean to look after the certification of travel and what the consequences were going to be. We asked the United States Public Health Service to perform this service for us, which they did very gladly and very well, although it was an extremely burdensome thing all round. The certificates were, I think, of some value; at all events the notifications sent out by the U. S. Public Health Service were of use. What the situation in Maryland would have been if we had had an epidemic of poliomyelitis I do not know. Would we have been driven into strict quarantine measures, with border quarantine?

It must be a great satisfaction to Dr. Emerson at this time to think of how many things he has relieved our minds, and what a valuable addition his experiences of the past summer have been to the rest of us, especially his experience with the institutions and on the clinical and hospital management side.

DR. WILLIAM S. BAER: I have been much interested in the epidemic we have had here, particularly as the hospital Dr. Blake took for the treatment of the cases was one with which I was affiliated. We have had an opportunity to study about 104 cases that have come from the city. I was particularly struck with the number of facial cases we had. About 10% of our patients have had simply a facial paralysis. About 10% were cases of paralysis of the respiratory tract.

Turning to the orthopedic side of the question, I will say a few words as to the plan of treatment I think ought to be pursued. The therapeutic side of the treatment still seems to be in doubt as far as the intraspinal injection of fluid is concerned. We have not done any great amount of good in injecting serum either intraspinally or intravenously.

From the orthopedic point of view I have some rather definite ideas. In the first place the treatment would seem to be outlined by the pathological lesions which exist in the spinal cord, so far as the paralytic cases are concerned. In the spinal cord we have the anterior horn cells disabled in three ways—by virus, by effusion, and by hemorrhage. Those cells disabled by effusion are going to recover in a fairly short period of time, say from four to five months. Those cells disabled by hemorrhage will recover more slowly and take anywhere from nine months to a year and a half to recover. The cells poisoned by the virus are not going to recover at all. Consequently the mode of treatment from a surgical point of view is to realize those different stages. In the first stage the case ought to be absolutely at rest for a period of three or four weeks at least. Better, indeed, to put those muscles weakened by disease absolutely at rest, and if necessary to encase not only a limited portion, but sometimes the entire body in some sort of support.

After that period is over, one may begin in those children a mild amount of massage or muscle training. Care should be taken not to overdo the process, as one can do great harm to a weak muscle by trying to make it do too much work. In the second stage of the disease, which lasts anywhere from six months to a year and a half, precautions should be taken against deformities and contractions. During this period electricity and massage are also given, and in addition certain forms of appliances like the

Zander apparatus and Swedish massage should be used. These are much better given in a bath, and particularly given in a warm bath. One can do the work better when one has the buoyancy of the water and the weight is taken off the individual muscles.

The third stage is the operative stage for correction of the deformity. There are two forms of operation, nerve transplantation and muscle transplantation. The first I do not believe offers any hope, as the nerves are probably degenerated. In muscle transplantation in properly selected cases one has a very efficient procedure.

Following this epidemic there will be a great deal of work for the city of Baltimore in assisting in the carrying out of further methods to help these children to help themselves. Two-thirds of them are going to be cripples and a handicap on the city of Baltimore and the state of Maryland. Again, if proper work is to be done for them, proper hospital supervision will have to be provided and the proper amount of money for braces will have to be forthcoming.

DR. EMERSON: There is no one who has been in an official position in this country during the past who will not remember with gratitude the immediate and effective assistance of the officers of the United States Public Health Service. If anything has impressed the public with the necessity of Federal control over many more things than it has now, the experience of last summer should have given the last touch to that impression. There should be a Secretary of Health in the Federal cabinet. There is no question but that the direction of laws and policies should be largely assisted by the kind of service the Federal health officers are giving to localities and communities throughout this country.

I want to pay particular tribute to the physicians in the city of New York who willingly sacrificed their personal health and family practice for the sake of doing what we asked of them in the interests of public health. When you ask physicians in the dull season of the year to notify the Health Department and give over to hospitals their patients, you are asking of them a sacrifice that no other profession is called upon to make.

We could not find any difference in the racial evidences of the disease. It is merely that the colored people are socially isolated from a good many other people in the community. With us the Italians had it first, next the Jews, then the Poles, and the colored people came down last.

In the second week of July we began to have clinics for physicians and we had first-class men coming down to teach them the delicacies and intricacies of the clinical diagnosis of the disease. It was a great clinical opportunity. I believe that up to the present time we have had an instance of paralysis of every one of the cranial nerves.

As to second attacks of the disease, I personally know of none. I have not heard any such cases mentioned.

With regard to the question of opening the schools, I kept a record of poliomyelitis occurring in children between the ages of 6 and 14 during the first few weeks of school. We have a school population of 1,000,000 children. In the two weeks between the 17th of September and the 1st of October we had in the first week

16 children of school age with poliomyelitis, and in the second week, 18 children. The week before school opened we had 16 cases; the week school opened we had 18 cases; the second week, 16 cases; the third week, 5 cases; the fourth week, 5; the fifth, 11; the sixth week, 7; and the seventh week, 6 cases. There is no record that this disease becomes epidemic in schools. It does not pass readily under these conditions. We would have felt justified in opening the schools on time, but we could not influence public opinion to that extent.

It was interesting to see that in the hospitals, possibly owing to the season of the year, there was no epidemic among the 4500 taken from their homes. We had an occasional case of measles and a few of whooping cough, but none of the secondary cases of acute infectious disease such as usually come into hospitals for children under five.

With regard to the recognition of pre-paralytic cases I can add very little. The recognition will, of course, be more likely during an epidemic than at other times, and until we have a specific diagnostic test, we must trust to the clinical acumen and judgment of physicians of large experience. There are many able physicians in New York who feel that the spinal puncture is as nearly a specific test as we want, and that, taken with the clinical picture, it forms a very valuable aid. At present it is quite impossible for anyone to say positively that they have got a true non-paralytic case of the disease. The opinion is strong within the Department of Health that with a paralytic case and other children coming down without paralysis in a family or house you have a right to call such coincident cases "infantile paralysis."

As to meningeal irritation, it is worth while to remember the old English name of the disease "morning paralysis," derived from the fact that patients may go to bed perfectly well and wake up with the disease. I remember perfectly well seeing a boy going to work, who tripped and fell, picked himself up and fell again, and who had to be helped home. He obviously had no meningeal irritation and yet developed a typical and severe paralysis in the midst of apparent perfect health.

We had facial paralysis in about 25% of our patients.

The after-care of these patients has been given a great deal of attention in New York. We have a permanent central committee on after-care, and a so-called fund for braces, which is really used for all kinds of needs of these children. Every case on discharge is visited at once by a nurse, and in the central office of the after-care committee a record is kept of every case, so that some years from now we will know what the particular care of each child has meant. We have in the community now about 5000 children with a persistent paralysis. Six hundred of these will be almost permanently bedridden. Two thousand five hundred of them are unable to walk now and they must be taught, like the cardiac and the handicapped tuberculous patient, to work at a trade which will give them self-support.

The medical relief, the transportation, the hospital and dispensary care, the home visits and the education for self-support are all to be directed by the committee on after-care, which has the support and assistance of all the important medical and social relief agencies in the city.

JOHNS HOPKINS HOSPITAL BULLETIN.

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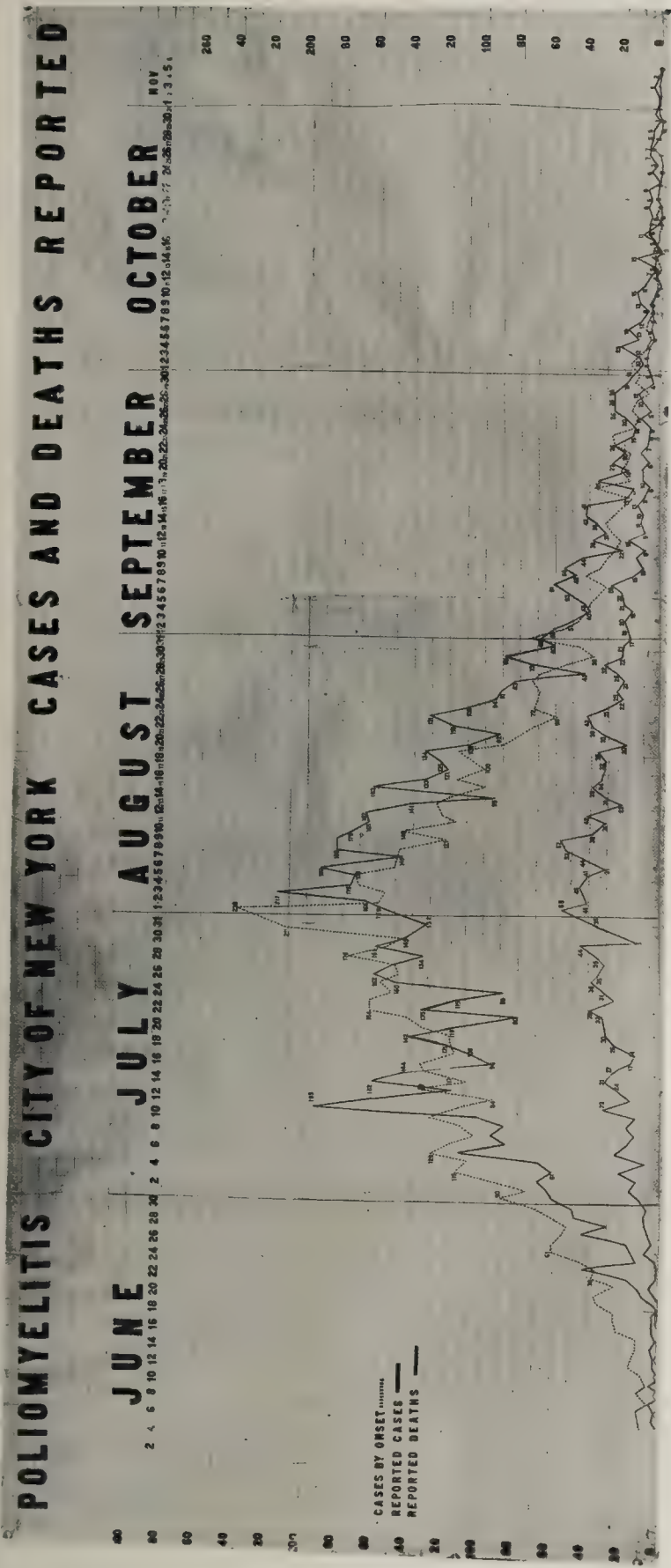


FIG. 1.—Cases and deaths reported, July to September, 1916.

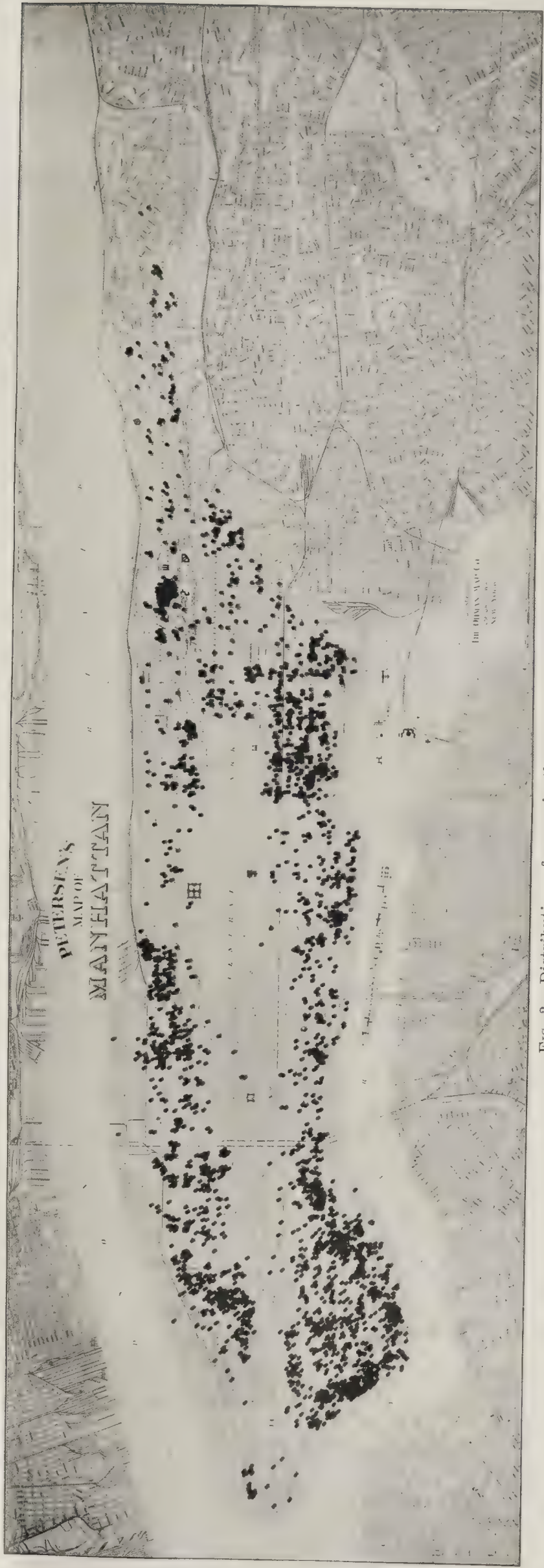


FIG. 2.—Distribution of cases in the Borough of Manhattan.

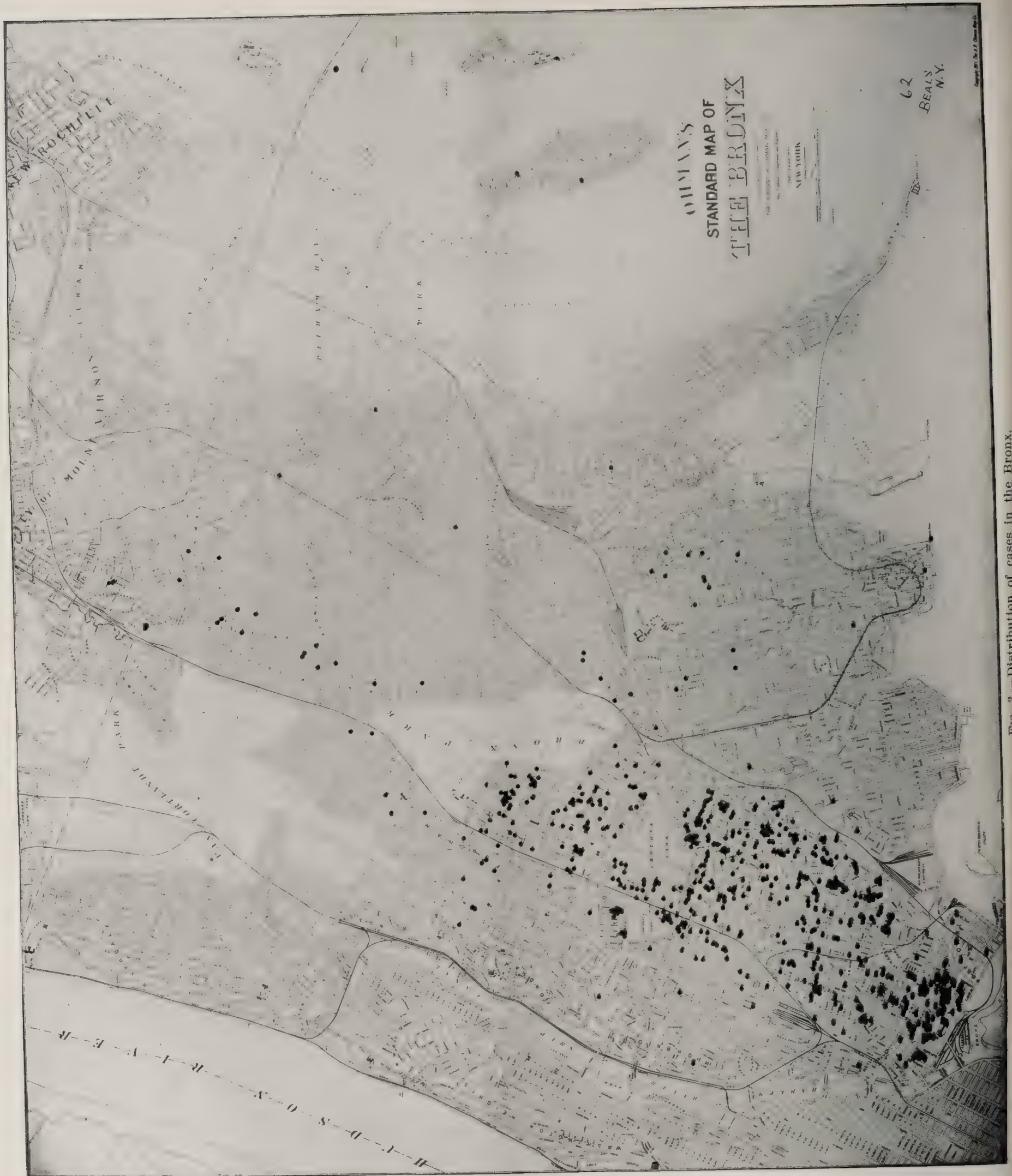


Fig. 3.—Distribution of cases in the Bronx.

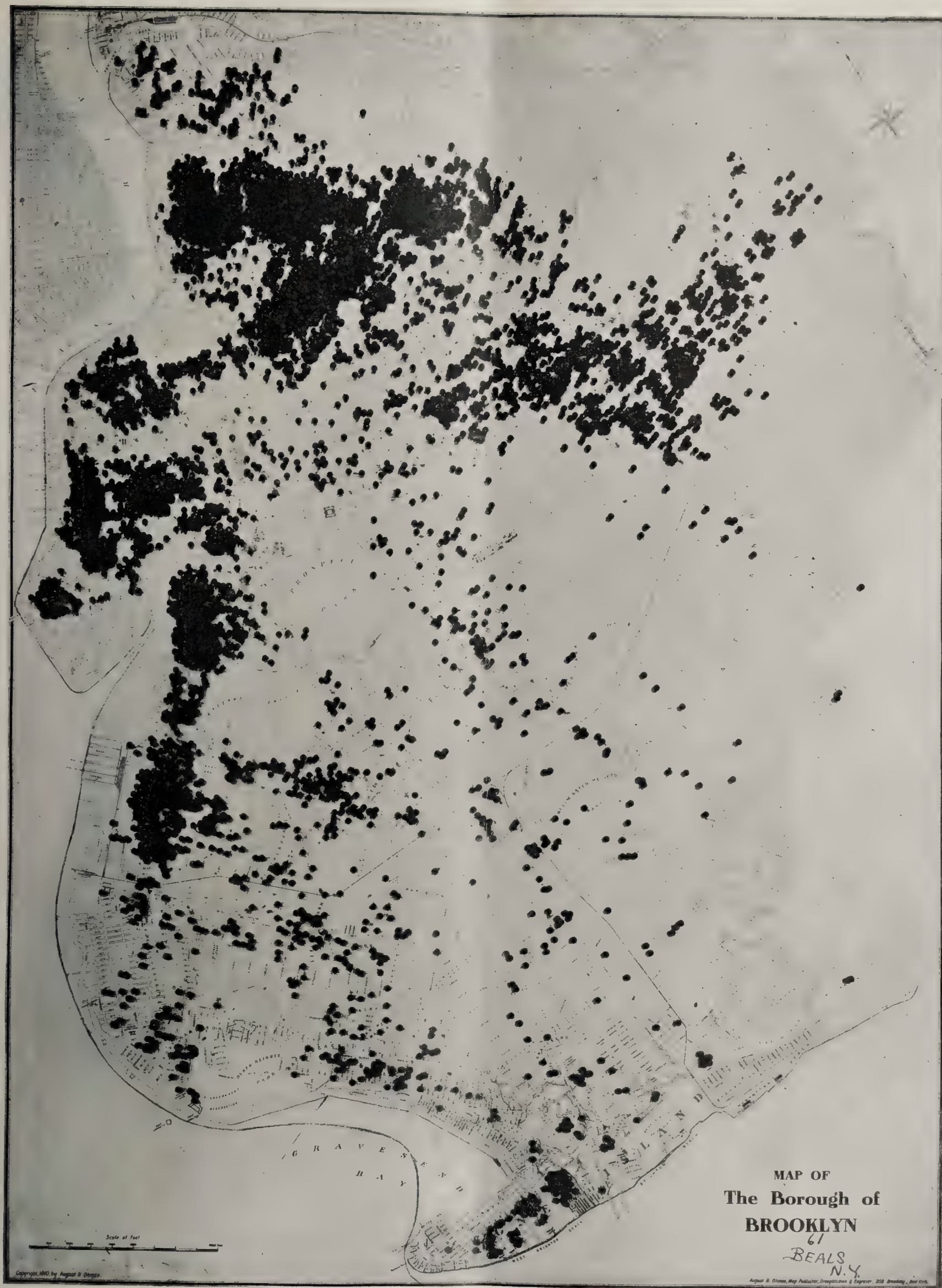


FIG. 4.—Distribution of cases in the Borough of Brooklyn.



FIG. 5.—Distribution of cases in the Borough of Queens.

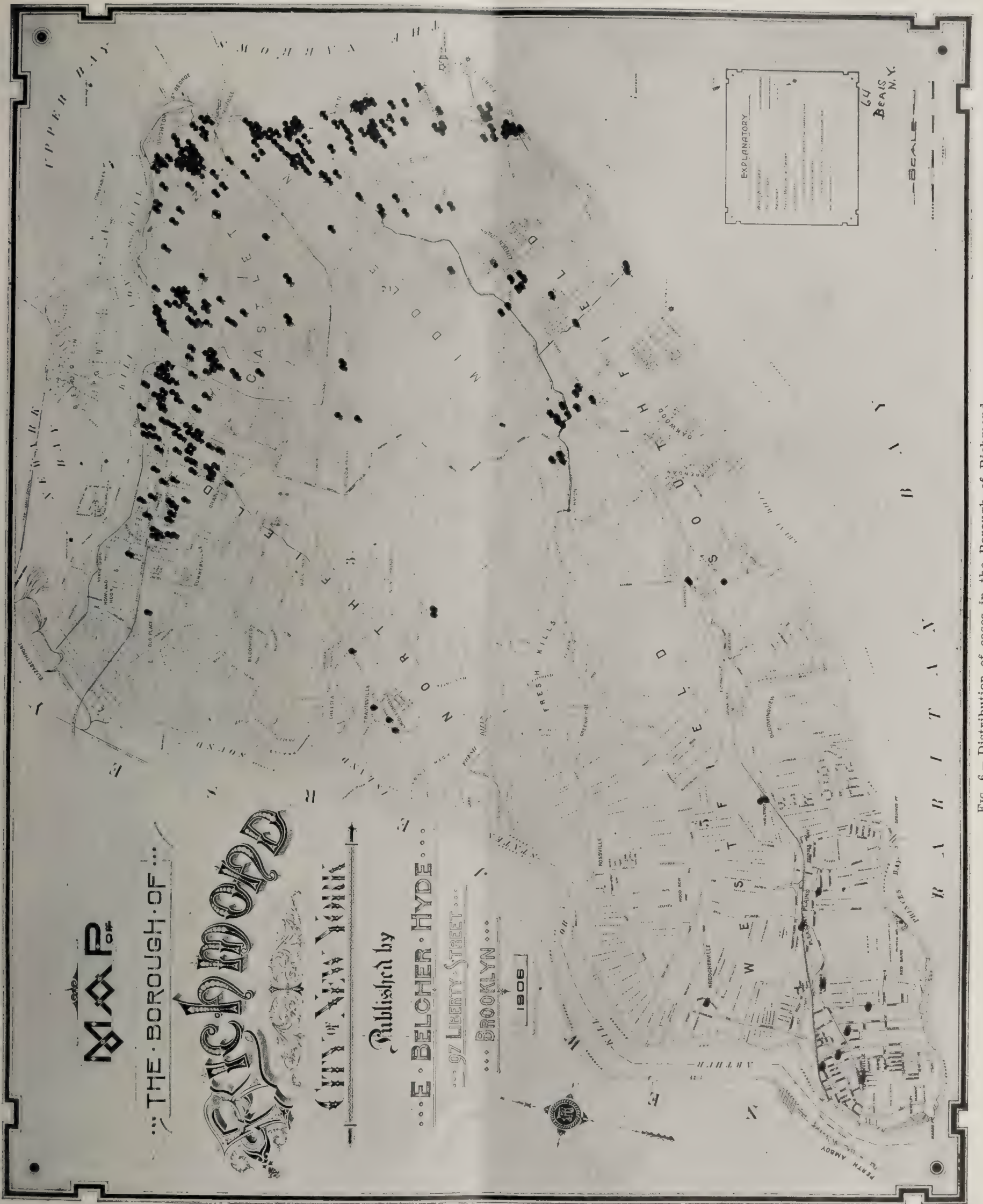


Fig. 6.—Distribution of cases in the Borough of Richmond.

PLACENTAL TRANSMISSION: CREATININE AND CREATINE IN THE WHOLE BLOOD AND PLASMA OF MOTHER AND FETUS.

By E. D. PLASS.

(From the Obstetrical Department of The Johns Hopkins University and Hospital.)

The recently developed methods for the quantitative determination of various constituents of normal blood have stimulated the study of the placental transmission of these substances with the hope of deducing some general principles involved in this reciprocal exchange which is so essential to the fetal economy. The relative concentration of a given substance in simultaneously collected samples of maternal and fetal blood should throw some light upon the method of interchange between the two circulations.

The blood is the vehicle by which the materials necessary for growth and repair are supplied to the cells and the waste products removed. The fetus must absorb the former from the maternal blood through the placental villi and may eliminate the latter through the same channel. Nature has endowed the fetal organism with remarkable attributes in order to avoid either a deficit of the essential building materials or a surplus of metabolic products. Clinical and chemical observations show that the growing fetus may store up materials that are badly needed by the maternal organism thus indicating either that the chorionic villi have a certain selective activity whose duty it is to provide the materials necessary for growth and that these pile up in the fetal blood, or that the growing fetal tissues have a greater chemical affinity for these substances and can abstract them from the circulating medium and even lead to a depletion of the maternal stores. The metabolic products that undoubtedly escape from the fetus into the maternal circulation theoretically belong in a different category but likewise must pass outward by simple diffusion or be actively eliminated by the villi.

According to the diffusion theory, the plasmas—the fluids on the two sides of the supposedly permeable membrane—should contain the same amounts of all soluble diffusible substances; whereas, according to the secretory theory, a difference in concentration of certain materials might occur on the two sides of the active membrane when their need was greater in one organism or when their presence was distinctly harmful. The various tissues of the fetus may bear a quantitative relationship to the concentration of a substance in the plasma which is quite different from the relationship existing on the maternal side of the placental barrier. Such a difference has been frequently observed in cases of anemia and osteomalacia where the maternal tissues are literally robbed of iron and calcium in order that fetal development may proceed normally. Such fetal parasitism has furnished the basis for arguments by the advocates of the secretory theory, whereas the underlying factor may well be a difference in affinity without any essential change in the actual transmission of materials. The plasma of the blood in the two circulations should be studied quantitatively by the methods available for the determination

of the various anabolic and catabolic materials, in the hope that this problem may be definitely settled.

Our insistence upon the use of plasma or serum values only in support of the diffusion theory of transmission is enforced by the difficulties encountered in the work to be reported on preformed and total creatinine. In the light of known facts it seems best not to consider the whole blood as a unit, as is so frequently done, but to look upon the corpuscular elements as distinct from the plasma. It is quite evident that the contents of the cells do not enter directly into the phenomenon of placental diffusion, but that in these problems the tendency to equalize concentrations must affect primarily the plasma. Many of the reported analyses for the various blood constituents indicate that the composition of the whole blood is quite different in many respects from that of the plasma.

Several chemical studies on placental transmission have recently appeared. Hymanson and Kahn⁸ analysed 12 specimens of maternal and fetal blood for the total lipoid content and for the cholesterol fraction, using whole blood for the former determination and serum for the latter. Their figures show no constant variation of either material in any one direction, although the average lipoid content is slightly higher in the fetal blood and the cholesterol somewhat lower than in the maternal. The differences are so slight and so inconstant as scarcely to warrant the conclusion which they draw "that the chorionic villi [seem to] have the function of discriminating which part and how much of each lipoid shall pass into the fetal circulation."

Slemons and Morriss,⁹ working with whole blood, determined the total non-protein nitrogen and urea in samples of maternal and fetal bloods collected at the time of delivery and found the same concentrations in both specimens. With no available data concerning the relation between the non-protein nitrogen of the whole blood and of the plasma or serum these figures prove less than they would if it were definitely known that equal concentrations were present in the blood cells and the surrounding plasma. A few scattered published analyses of the urea content of the whole blood and plasma, however, indicate that the concentration of this end-product of metabolism is the same in the cell elements as in the plasma and the figures for whole blood probably hold equally well for the plasma. The work of these authors, therefore, shows quite conclusively that urea passes the placenta by simple diffusion.

The work of Rabinovitch⁸ on the amino-acids cannot be advanced as evidence in favor of either theory. No note is made of analyses of simultaneously collected specimens but rather the conclusions are based upon the amino-acid content of the blood which flowed from the two cut ends of the cord. It was found that the blood from the fetal end had a higher

amino-acid value than that from the maternal end, thus indicating, Rabinovitch says, that the blood going from the fetus contains more $\text{NH}_2\text{-N}$ than that going toward the growing organism. The results as published are very inconclusive and quite contrary to the findings of Morel and Mouriquand as quoted by Slemons and Morriss.

Within the past month, Losee and Van Slyke have published in another connection four sets of determinations of the CO_2 -combining power of normal maternal and fetal plasma. The alkali reserve shows no significant variations, the fetus participating equally in the mild acidosis with which the mother is affected.

At the December meeting of the Society of Biological Chemists, Hunter and Campbell,⁴ in discussing the distribution of the creatinine and creatine between the corpuscles and plasma of the blood, gave the results of analyses for these two constituents in two sets of fetal and maternal plasmas. The values were the same in the two fluids and were similar to those reported here. These figures are the only ones available for these two materials and indicate that they maintain the same concentration in the two circulations. The work here reported was practically completed at the time the results of these two workers were presented.

In the present work the blood samples were collected as nearly simultaneously as possible and the analyses were begun at the earliest possible moment. The maternal specimens were taken from an arm vein and the fetal from the maternal end of the severed cord or from the distended umbilical vein by means of a needle. Bloods collected at night were preserved on ice until the following morning. When whole blood or plasma was used, coagulation was prevented by the addition of dry powdered potassium oxalate. Most of the analyses were done in duplicate and the color comparisons were always made by two individuals. All the samples were taken from patients who were delivered spontaneously at term. Asphyxiation of the child at birth was noted only once, in Case 13. Obstetrical chloroform anesthesia was usually employed, but in a few cases gas and oxygen were used and in two cases scopolamine-morphine analgesia. The anesthetic used had no influence upon the results. The parity and age of the mother and the duration of labor were likewise tabulated but showed no relation to the analytical findings.

As early as February 1916 a series of comparisons of maternal and fetal blood was begun, Folin's¹ method for creatinine and creatine being used. These earlier analyses (Table I) seemed to indicate that the problem was somewhat complicated. The preformed creatinine values are generally lower than those reported by Folin and Denis² for normal adults (1.1-1.4 mgm. per 100 c. c.); but show a close agreement between the maternal and fetal bloods. The total creatinine values are likewise lower than those of Folin and Denis, but the fetal bloods gave consistently higher results than the maternal. The differences in absolute values may possibly be explained by the use of deteriorated standard solutions of creatinine, but the comparisons are obviously not affected by this factor.

In the course of this work it was discovered that by hemolysing the blood before saturating it with picric acid higher values for both fractions were obtained. The greater hematocrit value of fetal blood was already known. A second series of determinations was now made, blood hemolysed by the addition of four volumes of distilled water, as suggested by Myers,³ being employed. The hematocrit values were obtained

TABLE I.—WHOLE BLOOD—NOT HEMOLYSED.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.		Fetal.	
	Preformed creatinine.	Total creatinine.	Preformed creatinine.	Total creatinine.
1	1.12	3.85	1.75	7.63
2	7.92	8.73
3	.54	4.19	.72	5.00
4	.90	4.80	.73	6.25
5	.93	4.31	.93	5.68
6	.56	4.68	.69	8.44
7	.62	5.48	.61	5.73
8	.61	4.43	.45	7.02
9	1.26	7.05	1.03	8.60
10	.84	7.05	.96	7.95
11	.80	5.68	.63	6.29
Average	.82	5.40	.85	7.73

by centrifugalizing the undiluted whole blood in 15 c. c. graduated centrifuge tubes for 20 minutes at 3000-3500 revolutions per minute. Satisfactorily pure picric acid was used and the colorimeter readings were corrected by a table similar to that published by Hunter and Campbell.³

The results (Table II) in general show less agreement between the two bloods than did the first series. The preformed creatinine varied in an inexplicable manner and,

TABLE II.—WHOLE BLOOD, HEMOLYSED.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.			Fetal.		
	Hemato-crit.	Preformed creatinine.	Total creatinine.	Hemato-crit.	Preformed creatinine.	Total creatinine.
8		1.12	4.59		1.08	6.72
12	22	3.75	9.55	41	5.24	11.45
13	31	5.29	6.98	41	4.47	8.17
14	30	2.26	5.66	35	2.34	6.18
15	24	1.41	6.00	25	1.87	6.94
16	28	3.37	8.28	35	3.03	10.42
17	25	1.98	8.71	33	3.85	10.72
18	28	1.98	8.33	39	3.00	9.68
19	34	1.55	7.54	34	2.52	9.40
20	33	1.16	6.84	36	2.64	9.50
Average	29	2.39	7.25	35	3.00	8.92

while the total creatinine roughly paralleled the hematocrit values, the relation was so inaccurate that no conclusions could be drawn regarding the comparative concentrations of the two constituents in the bloods.

It seemed that no relationship could be established and that further study would be profitless.* At this time a determination was made upon a sample of human blood plasma by Folin's original method; it was found not only that the total

* More recent observations by another method have indicated that the results for total creatinine in whole blood obtained by the Folin procedure are probably too high and that the variations cannot be taken as conclusive.

creatinine values were much lower but that the development of color in the picric acid filtrate after alkalization proceeded in a manner similar to that observed in the standard creatinine solutions. This suggested the use of plasma or serum in the study of the problem at hand and offered a new line of attack.

A third series of comparisons was consequently undertaken and a very definite relationship between the two bloods at once became apparent. The Folin method was employed as originally described. The lower total creatinine values make it advisable to make up the 10 c. c. portion of picric acid filtrate after autoclaving to 15 c. c. rather than to 25 c. c. and to read it against a 0.2 mgm. per 100 c. c. creatinine standard. If the serum or plasma shows hemolysis, the results may be disturbed as is shown in Table III. Oxyhemoglobin itself seems to be responsible for only a small part of the additional color development; the addition of small quantities of a solution of crystalline oxyhemoglobin to a standard solution of creatinine produces only a slight accentuation of the color developing after the addition of alkali. The injury to the cells which shows itself by the appearance of hemoglobin in the plasma apparently permits the escape of a reacting substance which disturbs the comparative results.

TABLE III.—DISCORDANT RESULTS WITH PARTIALLY HEMOLYSED PLASMA OR SERUM.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.			Fetal.		
	Hemolysis.	Preformed creatinine.	Total creatinine.	Hemolysis.	Preformed creatinine.	Total creatinine.
9	None	.87	1.85	Slight	.95	2.36
18	Slight	.85	2.14	Moderate	1.15	3.12
19	Marked	.86	3.63	Moderate	.92	2.77
20	None	1.11	1.59	Moderate	1.11	2.10
22	None	1.17	1.81	Moderate	1.15	2.33

The preformed creatinine values are little affected, but the total creatinine figures are considerably disturbed. This points to the presence of some substance which requires conversion by heat before it is able to give the color reaction. Creatine itself is in this category and moreover is in greater concentration in the corpuscles than in the surrounding plasma. In order to determine, if possible, whether the increased color development is due to creatine the following experiment was undertaken: Freshly drawn oxalated human blood was centrifugalized and clear plasma obtained; this was divided into two portions; to one part was added a good trace of cell extract obtained by adding distilled water to the original cell mass; the second portion was preserved clear. Routine Folin determinations were done on both portions and in addition the total creatinine was estimated by the acetic acid precipitation method.¹⁰ The following results were obtained:

	Picric-acid method.		Acetic-acid method.
	Preformed creatinine. (mgm. in 100 c. c.)	Total creatinine. (mgm. in 100 c. c.)	Total creatinine (mgm. in 100 c. c.)
Unhemolysed plasma	1.33	1.98	2.05
Hemolysed plasma	1.35	2.29	2.16

These results, as well as other observations, seem to indicate that most of the added color development which is noted in hemolysed serum or plasma is probably not due to creatine.

Nine pairs of fresh unhemolysed sera were secured and analysed by Folin's method (Table IV). Some difficulty was experienced in obtaining satisfactory specimens because of the great ease with which fetal blood hemolyses.

TABLE IV.—PLASMA OR SERUM.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.		Fetal.	
	Preformed creatinine.	Total creatinine.	Preformed creatinine.	Total creatinine.
4	.78	1.91	.85	1.95
10	.71	1.79	.78	1.95
21	1.38	1.91	1.30	1.93
23	.97	1.68	.96	1.63
24	1.22	1.82	1.07	1.88
25	1.14	1.61	1.14	1.86
26	1.25	1.85	1.03	1.93
27	1.17	1.85	1.14	1.97
28	1.31	2.32	1.33	2.28
Average	1.10	1.86	1.07	1.93

Preformed and total creatinine are present in practically the same concentrations in the maternal and fetal sera and the values obtained are constant within narrow limits. The preformed creatinine is the same as in normal non-pregnant women (1.0-1.2 mgm. per 100 c. c.) but somewhat lower than in normal men (1.3-1.5 mgm. per 100 c. c.). The total creatinine content of all normal human sera seems to be quite fixed (1.6-2.1 mgm. per 100 c. c.). The proportion in which the two components are present is variable, although the total remains the same. This corresponds with the observation that the urinary output of total creatinine is subject to only slight variations, although on occasion a portion of this total may be eliminated as creatine. Women and children are known to excrete creatine and it may be that the presence of this substance in the urine is dependent upon its higher concentration in the plasma.

Summary and Conclusions.—Simultaneously collected samples of maternal and fetal blood were analysed for preformed and total creatinine by Folin's method. The determinations on unhemolysed and hemolysed whole bloods brought out no definite information with regard to the exchange between mother and child, but when serum or plasma was used, a definite relation was clearly established. The concentration of both fractions is the same under normal conditions in the plasmas which are naturally the fluids concerned in the placental interchange.

The use of serum or plasma is essential in the study of placental transmission.

The plasmas of both mother and child contain the same amounts of preformed and total creatinine. The values are the same as those found in non-pregnant women.

The preformed and total creatinine apparently pass between the mother and fetus by simple diffusion.

I wish to express my thanks to the various house officers who have collected the specimens of blood and also to the Depart-

ment of Physiological Chemistry for the facilities and advice which have been given.

BIBLIOGRAPHY.

1. Folin, O.: On the determination of creatinine and creatine in blood, milk and tissues. Jour. Biol. Chem., 1914, XVII, 475.
2. Folin, O. and Denis, W.: On the creatinine and creatine content of blood. Jour. Biol. Chem., 1914, XVII, 487.
3. Hunter, A. and Campbell, W. R.: A hitherto neglected factor affecting the determination of minute quantities of creatinine. Jour. Biol. Chem., 1916, XXVIII, 335.
4. Hunter, A. and Campbell, W. R.: The distribution of creatinine and creatine between the corpuscles and plasma of blood. Proc. Soc. Biol. Chem., 1916.

5. Hymanson, A. and Kahn, M.: Lipoid content of maternal and fetal blood. Amer. Jour. Obst., N. Y., 1916, LXXIII, 1041.
6. Losee, J. R. and Van Slyke, D. D.: The toxemias of pregnancy. Amer. Jour. Med. Sciences, 1917, CLIII, 94.
7. Myers, V. C.: Chemical composition of the blood in health and disease. Post-Graduate, 1914, XXIX, 752.
8. Rabinovitch, K. N.: Contribution a l'étude de l'azote amino-acide dans le sang de la mère et du nouveau-né. (Observations sur des sujets humains.) Compt. rend. Soc. de Biol., 1914, No. 1, LXVI, 457.
9. Slemmons, J. M. and Morriss, W. H.: The non-protein nitrogen and urea in the maternal and fetal blood at the time of birth. J. H. H. Bull., 1916, XXVII, 343.
10. Wilson, D. W. and Plass, E. D.: Unpublished observations.

THE OBSTETRICAL SIGNIFICANCE OF THE BLOOD-SUGAR WITH SPECIAL REFERENCE TO THE PLACENTAL INTERCHANGE.

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Blood-sugar estimations were begun in this laboratory as part of a plan to study the problem of the placental interchange by systematic comparison of the various constituents of the blood of the mother and her newborn infant. It soon became apparent that analysis of the mother's blood was required not only at the conclusion of labor but also during the periods preceding and following the infant's birth. And finally, observations were made upon pathological cases.

Before the specimen for analysis was secured, the patient had fasted for at least three hours, a period which Hopkins and Graham found sufficient to eliminate errors due to alimentary glycosuria. The analytical method of Lewis and Benedict was adopted; for this has been widely used and has proved to yield consistent results. Since its initial step—dilution of the blood with water—insures thorough hemolysis, the estimation includes the sugar in both corpuscles and plasma. Essentially, the subsequent steps are precipitation of the blood-proteins with picric acid, filtration and, after further addition of picric acid and sodium carbonate to the filtrate, the development of a red color by careful heating. The chemical reaction involved is the reduction of picric to picramic acid by glucose. Comparison of the color obtained with that of a standardized solution of picramic acid determines the amount of sugar in the blood.

In order to control the technique, observations were made upon several individuals with normal carbohydrate metabolism. The results were within the normal limits described by Lewis and Benedict (0.09-0.11%) which are somewhat higher than those obtained by older methods. This fact must be taken into account when my determinations are compared with the results of previous investigators. Probably, the latter are somewhat too low, for the critical studies of McDanell and others have confirmed the accuracy of the Lewis-Benedict method.

BLOOD-SUGAR DURING PREGNANCY.

Until suitable analytical methods were devised, it was supposed that hyperglycemia existed during pregnancy, or at

least during the latter half of this period. The inference seemed to be justified by a number of clinical and experimental considerations. From the respiratory exchange in rabbits, Bohr concluded that glycogen alone supplied the energy required for embryonic development. A similar importance was then attributed to the carbohydrates in the development of the human fetus, and consequently, an increase in the maternal blood-sugar was expected. Furthermore, the susceptibility of pregnant women to alimentary glycosuria, as well as the results when epinephrin was administered, made the suspicion stronger that hyperglycemia existed. Yet, this is not the case; in uncomplicated pregnancy the blood-sugar is normal. This conclusion, reached by several investigators, is confirmed by my analyses of the blood in 11 patients at various periods of gestation.

BLOOD-SUGAR DURING PREGNANCY.

No.	Age.	Gravida.	Pregnancy.	Glyco-suria.	Blood-Sugar.	Remarks.
1	32	VII	2nd month.	0	0.098	Normal Pregnancy.
2	22	II	3rd "	0	0.119	Twins: aborted at fourth month.
3	21	I	3rd "	0	0.113	Neurotic vomiting, recovery.
4	22	I	6th "	0	0.102	Normal pregnancy.
5	22	II	7th "	0	0.095	Normal pregnancy.
6	22	I	7th "	0	0.107	Normal pregnancy.
7	19	II	7th "	0	0.10	Normal pregnancy.
8	29	I	7th "	0	0.099	Syphilis. Wassermann +++.
9	25	II	7th "	0	0.149	Very neurotic.
10	26	I	8th "	+	0.095	Mild, transitory glycosuria.
11	21	II	9th "	0	0.116	Normal and near term.

Only in the case (No. 9) of an extremely neurotic woman who was greatly alarmed by the preparations for securing a specimen of blood was hyperglycemia noted. Normal values obtained in cases of twins, hyperemesis, syphilis, and alimentary glycosuria. Excluding these, the mean value for the blood-sugar in six uncomplicated cases was 0.103% (the extremes were 0.116% and 0.098%). These results agree with the findings of a number of investigators collected in the following table, in which the average is 0.09%.

The significance of a normal blood-sugar during pregnancy becomes clearer if certain facts about the urine are recalled. Spontaneous glycosuria (alimentary) appears in approximately 10% of pregnant women, and glycosuria may be induced during pregnancy much more readily than at other times. Thus, 100 grams of glucose administered to healthy individuals will not provoke glycosuria, but when this amount is ingested during pregnancy, according to Reichenstein, in 37.5% of the cases sugar appears in the urine. Analogous

SUMMARY OF BLOOD-SUGAR DETERMINATIONS IN PREGNANT WOMEN.

Investigator.	Maximum.	Minimum.	Mean.
Schirokauer.....	[%] *0.112	[%] *0.085	[%]
Kampf.....	0.079
Benthin.....	0.096	0.054
Bergsma.....	0.136	0.07	0.091
Frank.....	0.12	0.08	0.095
Neubauer and Novak.....	0.09	0.05
Jacobson.....	0.105	0.094	0.098
Morris.....	0.116	0.098	0.103

*Plasma.

results have been reported by von Jaksch, Lang, Hofbauer and by Ludwig and Payer; Stolper invariably found sugar in the urine of pregnant women after the administration of 100 gm. of glucose.

Similarly, a small dose of epinephrin causes glycosuria more frequently during pregnancy than at other times. Jäger noted it in 38% of his cases after the administration of 0.5 c. c. of adrenalin; and Christofolletti reports a similar incidence of glycosuria after the administration of 0.3 c. c.

Upon this evidence pregnant women are said to have a low tolerance for sugar; but although clinical experience abundantly supports this conclusion, the explanation is not found in the presence of a hyperglycæmia. Consequently, various other suggestions have been offered. In the predisposition to glycosuria during pregnancy some authorities see the evidence

and in one instance a patient under my care (No. 10) presented a definite but very small amount of glucose in the urine while the blood-sugar was 0.095%. On the other hand, in healthy individuals Hamman and Hirschmann found that sugar appeared in the urine only when the blood-sugar reached 0.17%. At least during the latter part of pregnancy the renal threshold for glucose is low.

In view of the activity of the mammary glands an increase in the blood-sugar was expected during the puerperium but, as in pregnancy, analysis of the blood has shown the incorrectness of confidently held hypotheses. Throughout the puerperium normal values for the blood-sugar are found. Cases selected to represent successive days after the birth present 0.119% as the highest value for the blood-sugar, 0.092% as the lowest and 0.109% as the mean value. Correspondingly, Bergsma found 0.094% as the average in 22 cases. These results indicate an almost identical level for the blood-sugar in the periods before and after the infant's birth. In other words the regulatory mechanism for carbohydrate metabolism in women maintains approximately the same amount of sugar in the blood when a fetus is nourished in the uterus, when an infant is fed at the breast, and when there is no requirement to supply glucose to a dependent organism.

During lactation, it is well known that lactose frequently appears in the urine, and traces of it have also been detected in the blood. When introduced into the circulation, its quantitative elimination by the kidneys indicates that the organism cannot use lactose; and Abderhalden has shown that, except in the digestive tract, there are no enzymes in the body capable of splitting this disaccharide. Therefore, when absorbed from the mammary glands lactose is treated as a foreign body and the kidneys excrete it promptly. Probably in this fact, we have the explanation for the absence of an appreciable increase in the blood carbohydrate during the puerperium.

BLOOD-SUGAR DURING THE PUERPERIUM.

No.	Age.	Para.	Puerperium.	Blood-Sugar.	Remarks.
				[%]	
1	26	I	1st day.	0.095	Normal Puerperium 7 hours post partum.
2	34	IV	2nd "	0.092	" "
3	19	I	2nd "	0.101	" "
4	23	I	3rd "	0.119	" "
5	22	III	3rd "	0.10	" "
6	28	III	4th "	0.116	" "
7	28	II	5th "	0.118	" "
8	26	IV	5th "	0.118	" "
9	20	I	6th "	0.118	" "
10	24	I	7th "	0.118	" "

of lowered ovarian function, and others the effect of an increase in the adrenal or pituitary secretion. Whatever the relation of the glands of internal secretion to the phenomenon, its immediate cause seems to depend upon the kidneys, which during pregnancy are somewhat more permeable for glucose. Advocates of this view include Novak, Porges, Schirokauer, Mann, Bergsma, and Frank. The last investigator observed glycosuria during pregnancy when the blood-sugar was normal;

MATERNAL BLOOD-SUGAR DURING LABOR.

These studies actually began with determinations of the sugar in the blood of women at the conclusion of the second stage of labor. As soon as the infant was born a sample of its blood was obtained and immediately a sample was also secured from a vein in the mother's forearm. The latter contained a larger amount of sugar than is generally considered normal. At first suspicion was attached to the use of a tourniquet in the technique for obtaining the mother's blood, but it proved unjustified, for identical values obtained whether this appliance was employed or not. Then, it became advisable to learn whether the method of analysis yielded results during pregnancy and the puerperium agreeing with those of previous observers. As normal values were found in both of these periods, analyses were then made during the early part of labor to determine more precisely when the hyperglycæmia appeared.

In 28 normal cases, the mean value for the maternal blood-sugar at the moment of birth was 0.132% (maximum 0.185%, minimum 0.089%). These results are approximately a third

greater than those obtained during pregnancy and the puerperium. For the explanation of the hyperglycæmia several clinical facts pertaining to the conclusion of the birth must be taken into account. Thus, the voluntary muscular effort which expels the fetus, the wrought-up mental state of the parturient woman

MATERNAL AND FETAL BLOOD-SUGAR AT THE MOMENT OF BIRTH.

No.	Age.	Para.	Duration of labor.	Duration 2nd stage.	Maternal glycosuria.	Blood-Sugar.		Remarks.
						Mother.	Fetus.	
1	22	I	11:55	1:35	0	0.143	0.124	Normal labor. Whiffs of chloroform.
2	31	I	27:30	1:10	0	0.135	—	Normal labor. Whiffs of chloroform.
3	20	I	10:15	1:10	0	0.097	0.10	Normal labor. Morphine and tyramine.
4	20	I	19:20	1:05	0	0.161	0.131	Normal labor. Morphine and tyramine.
5	26	I	54:05	3:40	0	0.128	—	Normal labor. Whiffs of chloroform.
6	19	I	18:25	2:20	—	0.137	0.141	Normal labor. Whiffs of ether.
7	19	I	11:45	1:20	—	0.125	0.108	Normal labor. Whiffs of chloroform.
8	26	I	5:10	?	—	0.155	0.112	Prolonged labor, nervous. Whiffs of chloroform.
9	29	I	13:00	0:50	0	0.142	0.106	Normal labor. Whiffs of chloroform.
10	20	I	25:30	1:00	+	0.155	0.124	Normal labor. Whiffs of chloroform.
11	33	II	4:05	1:00	—	0.126	0.11	Normal labor. No anæsthetic.
12	25	II	11:45	0:50	0	0.156	0.124	Normal labor. Whiffs of chloroform.
13	25	II	9:35	2:20	0	0.146	0.108	Normal labor. Whiffs of chloroform.
14	21	II	4:15	0:20	0	0.115	0.103	Normal labor. Whiffs of chloroform.
15	28	II	4:00	1:45	0	0.112	0.086	Normal labor. Whiffs of chloroform.
16	25	II	12:10	1:05	—	0.11	0.075	Normal labor. Whiffs of chloroform.
17	22	II	22:00	2:00	0	0.125	0.101	Normal labor. Whiffs of chloroform.
18	28	III	6:15	1:20	0	0.122	—	Normal labor. No anæsthetic.
19	24	III	6:20	Rapid	0	0.105	0.096	Normal labor. No anæsthetic.
20	22	III	13:30	0:15	0	0.126	0.105	Normal labor. Whiffs of chloroform.
21	36	IV	14:00	0:45	0	0.172	0.122	Normal labor. Whiffs of chloroform.
22	34	IV	4:00	0:50	—	0.124	0.095	Normal labor. Whiffs of chloroform.
23	29	IV	14:20	?	0	0.126	0.094	Normal labor. No anæsthetic.
24	34	V	2:15	?	0	0.123	—	Premature labor. No anæsthetic.
25	30	V	10:45	1:35	0	0.132	0.112	Normal labor. Whiffs of chloroform.
26	31	V	22:00	3:00	0	0.126	0.13	Normal labor. No anæsthetic.
27	23	VI	12:35	0:20	—	0.089	0.06	Normal labor. Whiffs of chloroform.
28	39	VIII	7:00	3:00	—	0.185	0.185	Normal labor. Whiffs of chloroform.

and the anæsthetic administered for the relief of the pain may, singly or together, increase the amount of sugar in the blood. How far each is concerned may not be determined accurately, though the effort has been made to secure evidence bearing upon the problem. However, in the first place, Is an increase in the blood-sugar characteristic of the whole period of parturition?

In five cases the maternal blood-sugar determination at the conclusion of the second stage was compared with another determination made previously, but after labor had begun. The interval between the observations varied from three to twenty-seven and a half hours. In no case did the earlier estimation indicate a hyperglycæmia; the values were practically identical with those during normal pregnancy. For the first stage the average was 0.093% and for the second stage 0.136%. The increase in the blood-sugar, which varies between 30 and 60 per cent, occurs during the latter part of labor and probably is confined to the second stage, the period in which the expulsion of the fetus takes place.

BLOOD-SUGAR VALUES IN THE FIRST AND SECOND STAGES OF LABOR.

Serial Number.	Duration of labor.	Duration 2nd stage.	Blood-Sugar.			Interval between analyses.	Remarks.
			1st stage.	2nd stage.	Difference.		
26	22:00	3:00	0.098	0.126	0.028	3:00	Normal labor. No anæsthesia.
17	22:00	2:00	0.088	0.125	0.037	3:30	Normal labor. Whiffs of chloroform.
16	12:10	1:05	0.081	0.11	0.029	6:30	Normal labor. Whiffs of chloroform.
30	16:00	4:00	0.105	0.164	0.059	15:45	Mid-forceps operation. Complete anæsthesia.
10	27:30	1:00	0.094	0.155	0.061	27:30	Normal labor. Whiffs of chloroform.

Certainly, if an anæsthetic was employed, its influence was one factor in the causation of hyperglycæmia. In most instances, as soon as the head reached the perineum, whiffs of chloroform were administered simultaneously with the uterine contractions; and after vulval dilatation began the analgesia was deepened to anæsthesia. The whole period of chloroform administration was half an hour or less, and the amount of the drug used was rarely more than two or three drachms.

Anæsthesia induced either with chloroform or ether causes hyperglycæmia. Heinberg found from 0.3 to 0.6% of blood-sugar associated with chloroform poisoning. With lighter anæsthesia, smaller amounts were observed but even under these circumstances Hersch and Reinbach found hyperglycæmia. Similarly, the first hour of ether anæsthesia is attended with a rise of 5 to 26% in the blood-sugar (McGingen and Rois), and if prolonged, there is a further rise representing from 32 to 89% (Epstein and Aschner). In general these findings are confirmed by my observations upon dogs, which add a noteworthy fact, namely, that with chloroform narcosis the maximal blood-sugar is attained during the early part of the anæsthesia.

For example, in one instance the blood-sugar estimations were as follows:

Control: Before the anæsthetic was started.. 0.154%
Half an hour after the anæsthetic was started. 0.252%
One hour after the anæsthetic was started.... 0.247%
Two hours after the anæsthetic was started.. 0.245%

If comparison is made between the analytical results when the patients were given chloroform and when they were not, we find further proof of the influence of the anæsthetic. In

six cases delivered without an anæsthetic the average blood-sugar was 0.122%, whereas the corresponding average for those who were given chloroform was 0.137%. Nevertheless, if an anæsthetic is not employed, a rise in blood-sugar occurs at the conclusion of labor and is illustrated by Case 26, in which the first analysis yielded 0.098% and that at the end of the second stage 0.126%. This increase, we believe, must be attributed to the voluntary muscular effort used in the expulsion period. The influence of the uterine contractions, which of course are involuntary, must be small or entirely absent, for the blood-sugar generally remains low during the time when cervical dilatation is in progress.

It is pertinent that in the study of the relation between muscular work and the sugar-content of the blood uniform results have not been obtained. Liefman and Stern and also von Moraczewski found that muscular effort caused an increase in blood-sugar, but Wieland found it decreased from 0.09% (normal) to 0.065%. In dogs, stimulating the muscle with the faradic current, Reasch found that in eight instances the blood-sugar rose, in four it fell, and once there was no change.

Indirect evidence such as my observations afford indicates that voluntary muscular effort during labor increases the blood-sugar. Thus, in the case of primiparous women, in whom the expulsive stage is relatively longer and the requisite effort relatively greater, the mean value for the blood-sugar was 0.138%; in multiparous women the corresponding average was 0.129%. Although the highest blood-sugar observed, 0.185% (Case 28), occurred in an 8-para it was associated with prolonged, severe expulsive pains and, consequently, chloroform was administered more generously than usual.

When the cases are grouped according to the duration of labor, the findings point toward a definite relationship between the voluntary muscular work and the percentage of sugar in the blood. (In eight cases in which labor continued less than seven hours the mean value for the blood-sugar was 0.123%, whereas in 20 cases with the labor lasting a longer time the mean value was 0.136%. Nevertheless, the blood-sugar does not always vary with the length of labor, for a higher value obtained in a case continuing five hours (No. 9) than in one continuing 54 hours (No. 5). More frequently, it seems that the determining factor is the length of the second stage, and this also is a more accurate measure of the voluntary muscular effort. Thus, the average blood-sugar, when the expulsive period lasted half-an-hour, was 0.108%, when it lasted from one to one-and-a-half-hours, 0.135%, and when it lasted two and one-half to three hours, 0.144%.

What part of the rise in blood-sugar should be attributed to emotional causes, it is impossible to estimate; but we are inclined to believe it is very small. Even when patients were excited and almost uncontrollable the blood-sugar has not been higher than in the case of multiparous women, whose previous labors had terminated successfully and who, therefore, in the present labor were relieved of serious concern.

At the conclusion of obstetrical operations, as would be expected, high values for the maternal blood-sugar are found, for generally to the effect of prolonged and vigorous muscular

effort is added the influence of an anæsthetic. Some idea of the rise in blood-sugar is given by the analytical results in a case of forceps (No. 30), in which in the first stage of labor there was 0.105% blood-sugar and at the time of the birth 0.164%. But the difference between these analyses is not

BLOOD-SUGAR IN ABNORMAL CASES. OBSTETRICAL OPERATIONS.

No.	Age.	Para.	Duration of labor.	Maternal glycosuria.	Blood-Sugar.		Remarks.
					Mother.	Fetus.	
29	23	I	20:45	0	0.14	0.132	Low forceps. Chloroform. Normal infant.
30	30	VII	16:00	0	0.164	0.123	Mid-forceps. Chloroform. Normal infant.
31	24	I	0	0.116	0.113	Mid-forceps. Chloroform. Normal infant.
32	34	IV	62:00	0	—	0.136	Breech extraction. Chloroform. Stillborn infant.
33	35	V	8:50	—	0.125	0.119	Version. Ether anæsthesia. Stillborn infant.
34	36	II	0	0.163	—	Vaginal hysterotomy. Eclampsia. Chloroform.
35	38	I	0	0.285	—	Cæsarean section. Chloroform. Pre-eclamptic toxæmia.

TOXÆMIA OF PREGNANCY AND ECLAMPSIA.

36	25	I	11:20	0	0.082	—	Albuminuria. Normal labor. Chloroform. Normal infant.
37	26	I	5:30	0	0.105	—	Albuminuria. Normal labor. Normal infant.
38	23	I	10:40	0	0.139	—	Albuminuria. Observation six hours post partum.
39	42	IX	0	0.221	0.058	Nephritic tox. Prem. separation of placenta. Stillbirth.
40	34	II	0	0.097	—	Eclampsia. Ante partum. 1 convulsion.
41	36	II	0	0.128	—	Eclampsia. Ante partum. Observation after 3 convulsions.
42	21	I	0	a) 0.151 b) 0.183	—	Eclampsia. Intra partum. 1 convulsion: a) before, b) after.
43	18	I	0	0.136	Eclampsia. Post partum. 12 convulsions.
44	33	IV	0	0.256	Eclampsia. Post partum. 3 convulsions.

OTHER ABNORMALITIES.

45	36	I	12:10	0	0.191	0.133	Imbecile mother. Normal labor. Chloroform. Premature infant.
46	23	I	17:15	0	0.215	—	Profound anæmia. Hb. 50%. Chloroform. Normal labor.
47	25	IV	48:00	0	0.082	—	Syphilis (Wassermann ++++) Normal labor. Infant alive.
48	24	I	11:55	0	0.144	0.127	Mitral stenosis and insufficiency. Chloroform. Normal infant.
49	20	I	3:00	0	0.113	0.092	Glycosuria during pregnancy. Chloroform. Normal infant.
50	21	I	17:40	0	0.159	0.168	Prolonged administration of nitrous oxide. Normal infant.
51	34	VII	3:40	0	0.143	a) 0.099 b) 0.096	Twins. (Double-ovum.) Normal infants at term. Chloroform.

greater than may obtain in normal cases with chloroform anæsthesia. On the other hand, practically a normal blood-sugar may exist after half-an-hour of complete anæsthesia (No. 31), and although unusual, this result resembles others obtained on normal cases (Nos. 14, 15, 16, 27). As in these instances no determinations for blood-sugar were made during the first stage, it is impossible to say whether a rise occurred

in the second stage, but in any case it was not sufficient to cause hyperglycæmia.

The hyperglycæmia in Case 35—an elderly primipara threatened with eclampsia—is attributable to the influence of the anæsthetic, for the operation was performed before the onset of labor and pre-eclamptic toxæmia causes no disturbance in carbohydrate metabolism (Nos. 36 and 37). Even with convulsions, provided the determination is not made immediately after an eclamptic seizure, the blood-sugar may be normal (No. 40). It is true, nevertheless, that prompt analysis after a seizure reveals a notable increase in blood-sugar. Upon one occasion in the study of an eclamptic patient, a specimen of blood was obtained shortly before a convulsion occurred and another just after the seizure. In the former the sugar was 0.151% and in the latter, 0.183%. For this rise the convulsion was responsible, but it is uncertain whether the muscular contractions or the nervous mechanism governing carbohydrate metabolism was the basic factor. Neubauer found that the blood-sugar curve in nephritic patients ran parallel with that of the blood pressure, and saw in this relationship the evidence of stimulation of the higher nerve centers. Similarly, hyperglycæmia associated with uræmia and with apoplexy, according to Weiland, is of central origin. Without denying such a possibility, my observations show that high arterial tension is not always accompanied by hyperglycæmia, for Case 37 with a blood-pressure of 205 mm. of mercury presented 0.105% blood-sugar.

The blood-sugar appears to reach a higher level in nephritic toxæmia than is common in eclampsia, though my observations have been too few for generalization. Thus, a patient (No. 39) whose clinical history warranted the diagnosis of nephritis presented 0.221% blood-sugar, whereas in five eclamptics the corresponding figures were 0.097%, 0.128%, 0.136%, 0.151% and 0.256%. All of these patients recovered and were discharged with the urine free from albumin. But there may be a relationship between the character of the acute renal injury and the level of the blood-sugar; and, if so, the more severe the damage to the kidney, the higher the blood-sugar. Benthin, too, found a low blood-sugar in eclampsia and gives as the extremes in nine cases 0.041% and 0.159%. Consequently, he believes that the underlying pathological changes in eclampsia have very little, if any, effect upon the blood-sugar, though convulsions, high arterial tension, and cerebral lesions may cause notable hyperglycæmia. This view, endorsed also by Bergsma is supported by my observations.

THE FETAL BLOOD-SUGAR AND THE PLACENTAL INTERCHANGE.

The fetal blood was obtained from the placental end of the severed cord. Duplicate analyses upon specimens so obtained and upon others aspirated from the umbilical vein yielded identical results. As it was evident that with either procedure the blood came from the umbilical vein, the simpler method of collecting the sample was adopted. Having just left the placenta on its way back to the fetus this blood was arterial. The structure of the umbilical arteries and their prompt con-

traction after the infant is born rendered unsuccessful the efforts to secure a sample of the blood passing from the fetus to the placenta. Comparison of the arterial and venous blood in the umbilical cord of dog-embryos showed a difference in sugar content, though only a small one and not beyond the limits of experimental error.

In 24 normal cases the mean value for the sugar in fetal blood was 0.115% (extremes 0.185% and 0.06%). Two-thirds of the analytical results were within the limits normal for adults, and the remaining cases presented slightly higher values. When the mother, under anæsthesia, was delivered by an operative procedure, the average for the fetal blood-sugar was 0.125%, a finding which suggests that generally an increase in the maternal blood-sugar is accompanied by a rise in the fetal. On the other hand, when the mother was not given an anæsthetic, the average fetal blood-sugar was 0.11%.

Two infants born prematurely at the 7th month presented 0.062% and 0.08% blood-sugar respectively. In three cases the blood of still-born infants at term yielded 0.058%, 0.119% and 0.135%. From these data, it appears, there is nothing characteristic in the percentage of blood-sugar in still-born infants.

Analyses of the blood of healthy new-born infants, comparable with those included in my normal series, have been recorded by Bergsma, who found 0.1065% the mean value in six cases, a figure not unlike my average in 24 cases. Older infants are said to present normal values (Bass, Mogwitz, Goetsky, Bing and Widelow), though Cobleiner found hyperglycæmia in late infancy.

From my analyses it appears that there is slightly more sugar in the maternal blood than in the fetal—a fact intimated by the averages 0.135% for the mother, 0.115% for the fetus, and borne out when the cases are studied individually. In 19 normal cases, the maternal values were higher; and in five they were practically identical with the fetal. The mean difference was 0.027% in favor of the maternal blood.

This difference, it seemed possible, was explained by the fact that the maternal sample was taken from a peripheral vessel. And to learn if this were true, animal experimentation was resorted to. In a non-pregnant dog under ether anæsthesia samples of blood were secured from the femoral vein and from the vena cava about the level of the uterine veins. The sugar-content of the former was 0.209% and of the latter 0.215%. These are equivalent analytical results. For our purpose, however, the results of a more crucial experiment are important.

In the case of a pregnant dog near term, under ether anæsthesia, laparotomy was performed and samples of blood were secured from a uterine vein and from the umbilical vein of the most accessible embryo. There was 0.139% blood-sugar in the maternal and 0.123% in the fetal blood. Obviously, these results duplicate the clinical observations upon women at the conclusion of labor and demonstrate that there is less sugar in the fetal blood than in the maternal when the latter is obtained from a uterine vein.

While the requisite conditions attending animal experimentation make it impossible to rule out the effects of the anæsthetic, this was accomplished clinically in several normal cases,

the patients declining to take an anæsthetic, (Nos. 11, 19, 23, 26). In three instances slightly more sugar was found in the maternal blood; in the fourth practically equal amounts were present in the two circulations. Hence it appears that, even when anæsthesia is not employed, the maternal blood is richer in sugar than the fetal blood, though the difference becomes greater when chloroform, ether, or nitrous oxide is administered.

From the results of his observations in six cases, Bergsma concluded that the sugar-content of the blood in mother and fetus is the same. But his work is open to criticism, for the specimens were not obtained simultaneously—between them at times there was an interval of twenty minutes. And as the maternal specimen was the last to be secured, the normal value found may merely indicate the rapidity with which the value for the blood-sugar falls at the end of the second stage.

With regard to the mechanism responsible for the passage of glucose from mother to fetus, comparison of the sugar content of the two circulations lends no support to the hypothesis requiring the action of an enzyme. This doctrine advocated by Hofbauer rests chiefly upon his demonstration of glycolytic ferments in glycerine extracts of the placenta. Their function, it may well be, is the preparation of glycogen, stored in the placenta, for passage to the fetus; but, as I have said, the results of blood analysis certainly do not indicate that they or other enzymes effect the transmission of glucose through the organ. Indeed, they rather speak against it. Thus, in a case of double-ovum twins, where each fetus acquired its food-stuffs through a separate placenta, the blood-sugar of one was 0.099% and of the other 0.096%. It is difficult to imagine such equality if an enzyme action is responsible for the transmission of the glucose, whereas equality would be expected if diffusion is responsible.

In animals* with hyperglycæmia, artificially induced, Cohnstein and Zuntz proved that glucose passed through the placenta in accord with the laws of diffusion. The data in my series of cases indicate that this process also accounts for the transmission of glucose to the human fetus.

FETAL AND MATERNAL BLOOD-SUGAR.

(In cases where two observations were made upon the mother.)

First stage.	Second stage.	Fetal.	Remarks.
%	%	%	
0.094	0.155	0.124	Normal labor. Chloroform.
0.081	0.11	0.075	" " "
0.088	0.125	0.101	" " "
0.098	0.126	0.13	" " No anæsthetic.
0.105	0.164	0.123	Mid-forceps. Complete anæsthesia.

If the determinations upon the fetal blood are compared with those upon maternal blood during the early part of labor, the latter with one exception are the lower. On the other hand, at the moment of birth the maternal values are generally somewhat higher than the fetal; occasionally the same values

obtain in both organisms. Probably, as the concentration of sugar increases in the maternal blood, that in the fetal blood also rises. With diffusion the responsible mechanism for the placental transmission, this result would be expected. Furthermore, the difference, noted both clinically and experimentally between maternal and fetal values, is in full accord with a diffusion process; the higher maternal concentration insures the flow of glucose toward the fetus.

As normal values appear in pregnant women the maintenance of a suitable amount of carbohydrate in the fetal circulation does not depend upon a maternal hyperglycæmia. Consequently, if diffusion is the process responsible for a suitable supply of glucose to the fetus, relatively lower sugar values would be expected in the fetal blood. Such are actually found. At the conclusion of labor the concentration of glucose in the fetal blood is approximately 12% lower than in the maternal blood.

These findings suggest a prompt disposal of glucose on the part of the fetus, which may depend either upon rapid oxidation or upon unusual facilities for storage. To some extent the first possibility is discredited by the results of my experiments to determine the relative rapidity of glycolysis in the two circulations. When samples of maternal and fetal blood were placed in a thermostat at 38° C. and determinations made from time to time, it appeared that the sugar decreased in both at the same rate. Similar experiments will be made, corresponding organs of the adult and the new-born infant being employed. But in any event probably a great facility for storage of carbohydrate in the fetus is an important factor in maintaining its level of blood-sugar relatively lower than the mother's.

CONCLUSIONS.

1. Normal blood-sugar values (0.09-0.11%) prevail during pregnancy and the puerperium.
2. During the early part of labor the values are normal, but in the second stage the blood-sugar is increased. In 28 cases at the moment of birth the average maternal blood-sugar was 0.132%.
3. The rise in the blood-sugar is partly due to the mother's voluntary efforts to expel the fetus, and it is accentuated by the use of an anæsthetic.
4. At the moment of birth the fetal blood-sugar is lower than the maternal. In 24 normal cases, in most of which an anæsthetic was used, the average fetal value was 0.115%.
5. The concentration of glucose in the two circulations is such that the placental interchange may readily be explained by the process of diffusion; and the lower concentration in the fetal blood assures a flow of glucose from mother to fetus.
6. After obstetrical operations higher values are found for the blood-sugar in both mother and fetus, and are explained by the influence of the anæsthetic.
7. Normal blood-sugar values prevail in pre-eclamptic toxæmia though a rise occurs just after a convulsion. Also after repeated convulsions or with pronounced renal involvement the percentage of blood-sugar may be notably increased.

* For these experiments guinea-pigs and a cat were used; a solution of glucose was introduced intravenously.

LITERATURE.

Abderhalden: Quoted from Liepmann. Handbuch der Frauenheilkunde. Leipzig, 1914, III, 155.

Bang, I.: Der Blutzucker, Wiesbaden, 1913.

Bass: The sugar content of blood in childhood. Am. J. Dis. Child., 1915, IX, 63.

Benthin: Der Blutzuckergehalt in der Schwangerschaft, in der Geburt, im Wochenbett, und bei Eklampsie. Zeitschr. f. Geburtsh. u. Gynäk., Stuttgart, 1912, LXXI, 544.

Bergsma: Der Zuckerstoffwechsel in der Schwangerschaft und im Wochenbett. Ein Beitrag zur Frage der Schwangerschaftsleber. Ztschr. f. Geburtsh. u. Gynäk., Strassb., 1912, LXXII, 105-153.

Bing u. Widelow: Blutzuckerbestimmungen bei Kindern. Ztschr. f. Kinderh., 1913, IX, Nr. 1.

Bohr: Skand. Arch. f. Physiol., 1900, X. Quoted from Marshall. Physiology of Reproduction. Longmans & Co. p. 434.

Christofolletti: Quoted from Liepmann. Handbuch der Frauenheilkunde, Leipzig, 1914, Band III, p. 155.

Cobleiner: Blutzuckeruntersuchungen bei Säuglingen. Ztschr. f. Kinderh., 1910, I, 207.

Cohnstein and Zuntz: Weitere Untersuchungen zur Physiologie des Säugethier-Fötus. Pflügers Arch., 1888, XLII.

Epstein and Aschner: The effect of surgical procedures on the blood-sugar content. Journ. Biol. Chem., 1916, XXV, 151.

Frank: Weitere Beiträge zur Physiologie des Blutzuckers. Ztschr. f. physiol. Chemie, Strassb., 1910, LXX, 299.

Goetzky: Der Physiologische Blutzuckergehalt beim Kinde nach der Mikromethode von Bang. Ztschr. f. Kinderh., 1913, IX, Nr. 1.

Graham: Variations in the Blood-Sugar in Health. Journ. of Physiology, London, 1916, I, 285-295.

Hamman and Hirschmann: The Renal Threshold for Glucose. An Abstract of the Proceedings of the Eighth Annual Meeting. The American Society for Clinical Investigation, 1916, p. 27.

Heinsberg: Dissertat. Würzburg, 1895.

Hirsch u. Reinbach: Ueber psychische hyperglycämie und Narkosehyperglycämie beim Hund. Ztschr. f. physiol. Chem., Strassb., 1914, XCI, 292.

Hofbauer: Biologie der mensch. Placenta, 1905.

Hopkins: Blood-Sugar in Health. Am. J. M. Sc., 1915, CXLIX, 254.

Jacobson. Untersuchungen ueber den Einfluss verschiedener Nahrungsmittel auf den Blutzucker bei normalen, Zuckerkranken, und graviden Personen. Biochem. Ztschr., Berl., 1913, LVI, 471-494.

Jäger: Quoted from Liepmann: Handbuch der Frauenheilkunde. Leipzig, 1914, Band III, 155.

Jaksch (von): Quoted from von Winckel. Handbuch der Geburtshilfe. Wiesbaden, 1903, Band I, Hft. I, p. 404.

Kampf: Inaug. Dissert., Halle, 1908.

Lanz: Quoted from von Winckel. Handbuch der Geburtshilfe. Wiesbaden, 1903, Band I, Hft. I, 405.

Lewis and Benedict: A method for the estimation of sugar in small quantities of blood. J. Biol. Chem., 1915, XX, 61-73.

Liefmann u. Stern: Ueber Glykämie und Glykosurie. Biochem. Ztschr., Berl., 1906, Bd. I, 299-308.

Ludwig and Payer: Quoted from von Winckel. Handbuch der Geburtshilfe, Wiesbaden, 1903, Band I, Hft. I, p. 404.

McDanell, Louise: The estimation of sugar in the blood by the Lewis-Benedict method. A graph for obtaining directly the percentage of dextrose. Journ. of Lab. & Clin. Medicine, I, No. II.

McGuigan and Rois: Liver circulation and glycæmia. Am. J. Physiol., 1915, XXXIX, 480.

Mann: Die Schwangerschaftsglykosurie, eine Form des renalen Diabetes. Ztschr. f. klin. Med., Berl., 1913, LXXVIII, 488-500.

Mogwitz: Ueber den Blutzucker der Säuglinge. Monatschr. f. Kinderh., Leipz. u. Wien., 1914, XII, 569.

Moraczewski (von): Ueber den Einfluss der Muskelarbeit auf den Blutzucker. Berl. klin. Wchnschr., 1915, LII, 1038.

Neubauer: Ueber Hyperglykämie bei Hochdrücknephritis und die Beziehungen zwischen Glykämie und Glykosurie beim Diabetes Mellitus. Biochem. Ztschr., Berl., 1910, XXV, 284-295.

Neubauer u. Novak: Zur Frage der Adrenalinämie und des Blutzuckers in der Schwangerschaft. Deutsche Med. Wochenschr. Leipz. u. Berl., 1911, XXXVII, 2287-2289.

Novak, Porges, u. Strisower: Ueber eine besondere Form von Glykosurie in der Gravidität und ihre Bezeichnungen zum echten Diabetes. Ztschr. f. klin. Med., Berl., 1913, LXXVIII, 413-453.

Reasch: Quoted from I. Bang. Der Blutzucker. Wiesbaden, 1902.

Reichenstein: Glykosurie und Schwangerschaft. Wien. klin. Wchnschr., 1909, XXII, 1445.

Alimentare Glykosurie und Adrenalinglykosurie mit besonderer Berücksichtigung der Glykosurie in der Gravidität und der Zuckerkrankheit. Wien. klin. Wchnschr., 1911, XXIV, 862.

Schirokauer: Zum Zuckerstoffwechsel in der Schwangerschaft. Berl., klin. Wchnschr., 1912, XLIX, 500.

Slemons and Morriss: The non-protein nitrogen and urea in the maternal and fetal blood at the time of birth. Bull. Johns Hopkins Hospital, Baltimore, 1916, XXVII, pp. 343-368.

Stolper: Quoted from Liepmann. Handbuch der Frauenheilkunde. Leipzig, 1914, III, 155.

Weiland: Oekonomie des Blutzuckers. Zntalbl. f. d. ges. Phys. u. Path. d. Stoffwechsels, Berl. u. Wien, 1910, n. F., V, 481.

CHANGES IN THE BLOOD PICTURE AFTER NUCLEIC ACID INJECTIONS.

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During the last decade many workers¹ have reported, some favorably and others unfavorably, concerning the therapeutic action of nucleic acid in those diseases which theoretically ought to be influenced by an increase of the leucocytes. It is not the purpose of this report to discuss this issue, but rather to direct the reader's attention towards some changes in the blood picture which we believe ought not to be neglected, especially when repeated injections of nucleic acid are given.

Schittenhelm and Bendix,² using the rabbit as an experimental animal, found that nucleic acid in itself was not very

toxic and that it was very slow to be absorbed. When it was injected subcutaneously or intramuscularly, indurations resulted. Intravenous injections, except in minute quantities, caused acute nephritis.

As we had the treatment of patients in view primarily, the use of intravenous method of application was precluded. We also employed rabbits in our first test work, using the sodium salt of nucleic acid, and adding to this sodium cinnamate, arsenic, and quassia, according to the formula originated by Lundvall,³ and recently recommended for the treatment of

dementia præcox by Bayard Holmes.⁴ The mixture is made according to the following prescription, which from now on we shall refer to as Lundvall's solution:

Quassini depurati sicci.....	2.0
Aquæ destillatæ bullientis, q. s. ut fiat.....	50.0
Boil in a water bath for one and a half hours, filter, and add	
Hetoli (<i>i. e.</i> , sodii cinnamati).....	1.0
Sodii nucleinati	10.0
Acidi arsenosi (in solution).....	0.005
Boil until all is dissolved, filter, and add	
Aquæ destillatæ bullientis, q. s. ut fiat.....	50.0

This solution, which contains the two strongest known agents for producing leucocytosis, namely sodium nucleinate and hetol, together with arsenic and quassia, was injected into the thighs of four healthy rabbits. The temperature of these animals had been taken, the leucocytes and the erythrocytes had been counted, and the hæmoglobin had been determined daily for a week previous to the experiments. All of them showed practically no fluctuation of these four factors previous to the injection of 1 c. c. of Lundvall's solution. Then the animals gave evidence of extreme pain. This was especially noted during and directly following the injection. The temperature first fell, then gradually rose about one degree above normal, during the first sixteen hours after injection. The number of erythrocytes and leucocytes and the percentage of hæmoglobin fell twenty-four hours after the injection. The red blood corpuscles decreased about a million, the white about two thousand and the hæmoglobin five to ten per cent. Forty-eight hours after the injection the red count had again reached the normal height, but it took the animals a week to recover their normal percentage of hæmoglobin. The white count, in which we were especially interested, rose perceptibly above normal in only two animals. In one an increase of six thousand lasted two days, in the other an increase of from three to four thousand lasted nine days. These results were not encouraging, but thinking that the fault might lie in the lack of absorption due to the induration at the point of injection, we next experimented with cats, carnivorous animals, which we thought might give a different reaction.

Four cats were consequently injected with 1 c. c. of the solution; their weight, averaging 2.5 kilograms, was about equal to the average weight of the rabbits. Their reactions, as regards pain and temperature, were not different from those of the latter animal. The red count and the percentage of hæmoglobin showed less tendency to drop, and in the two cases in which there was a slight drop the animals recovered rapidly within twenty-four hours. The maximal leucocytosis occurred three days after injection. There was an average increase of eleven thousand leucocytes. In one case an increase of eighteen thousand was recorded. These increases lasted about eight days, declining step-like from day to day, as can best be seen on curve No. 1, a fair example of the curves obtained.

A second injection of 1 c. c. of Lundvall's solution, after the count had come down to normal, gave a slight increase of the leucocytes in one animal; this leucocytosis of from two to

three thousand lasted a week. A second injection of 2 c. c. of the solution, in another animal gave no increase at all (Curve No. 1).

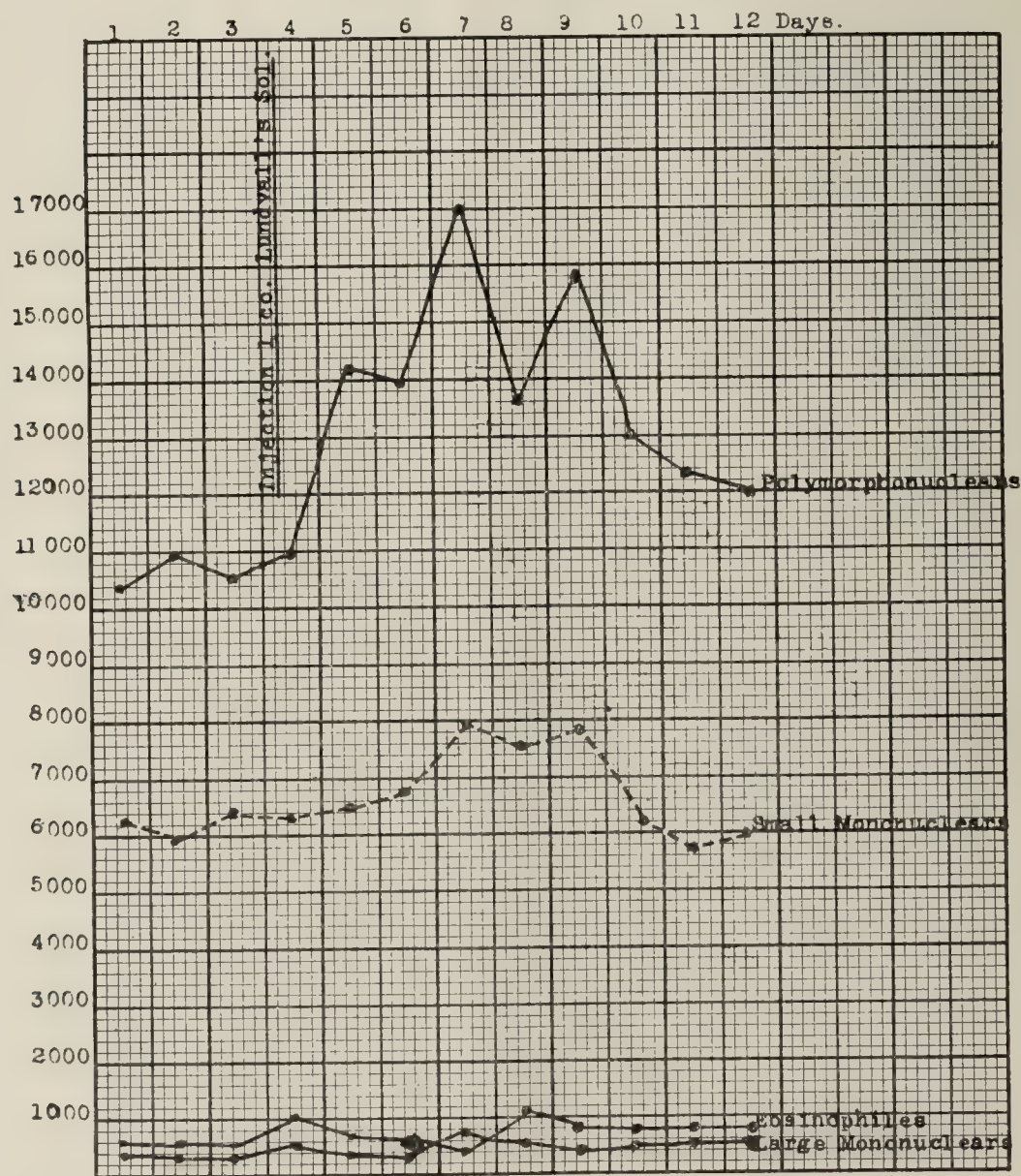
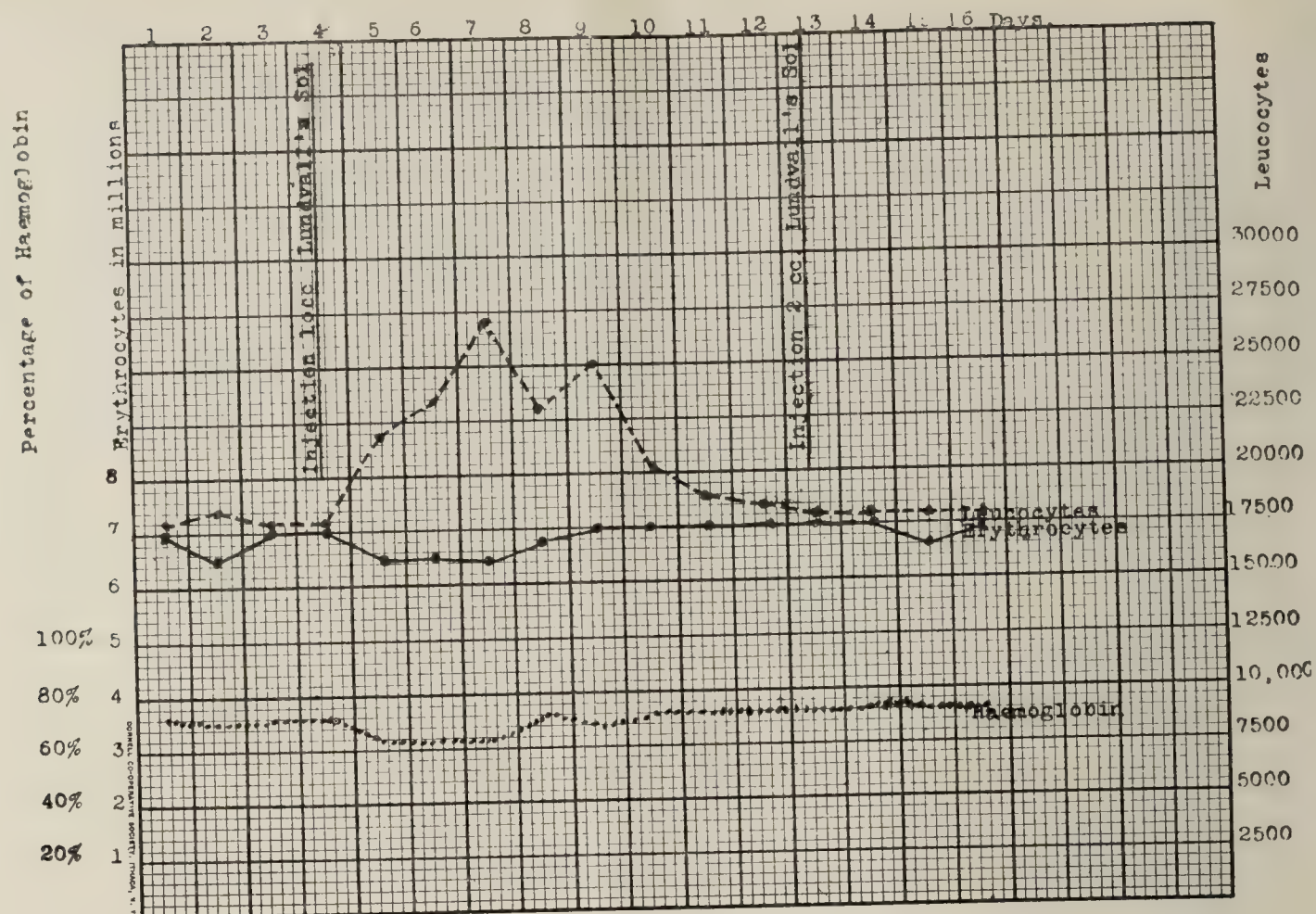
Differential counts (Curve No. 2) showed a relative increase of the polymorphs and eosinophiles compared to the small and large mononuclears. No pathological elements were observed. Busse⁵ called attention to this relative increase of leucocytes over lymphocytes in patients treated with nucleic acid alone; Landerer,⁶ working with hetol, demonstrated an eosinophilia in his patients.

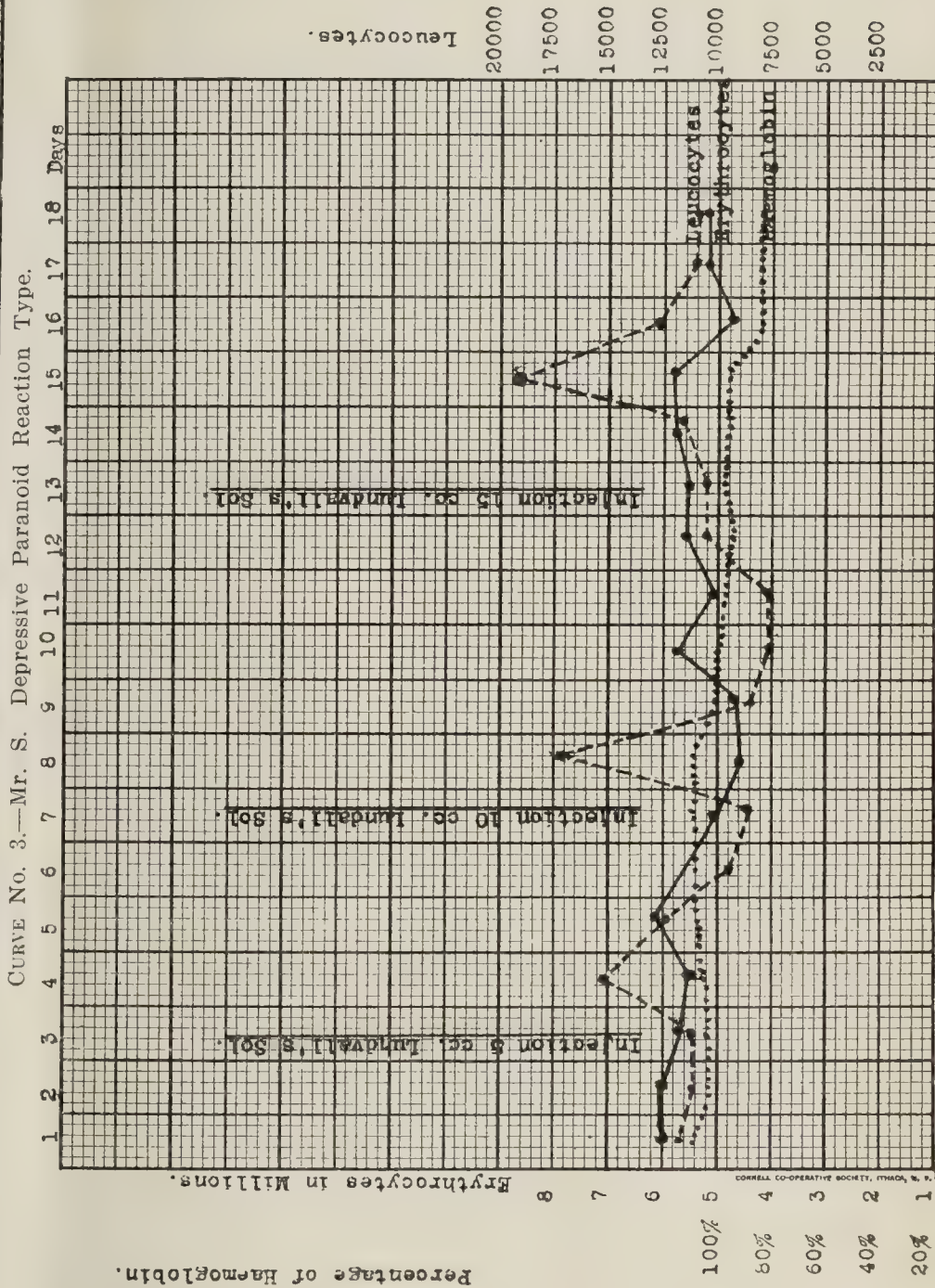
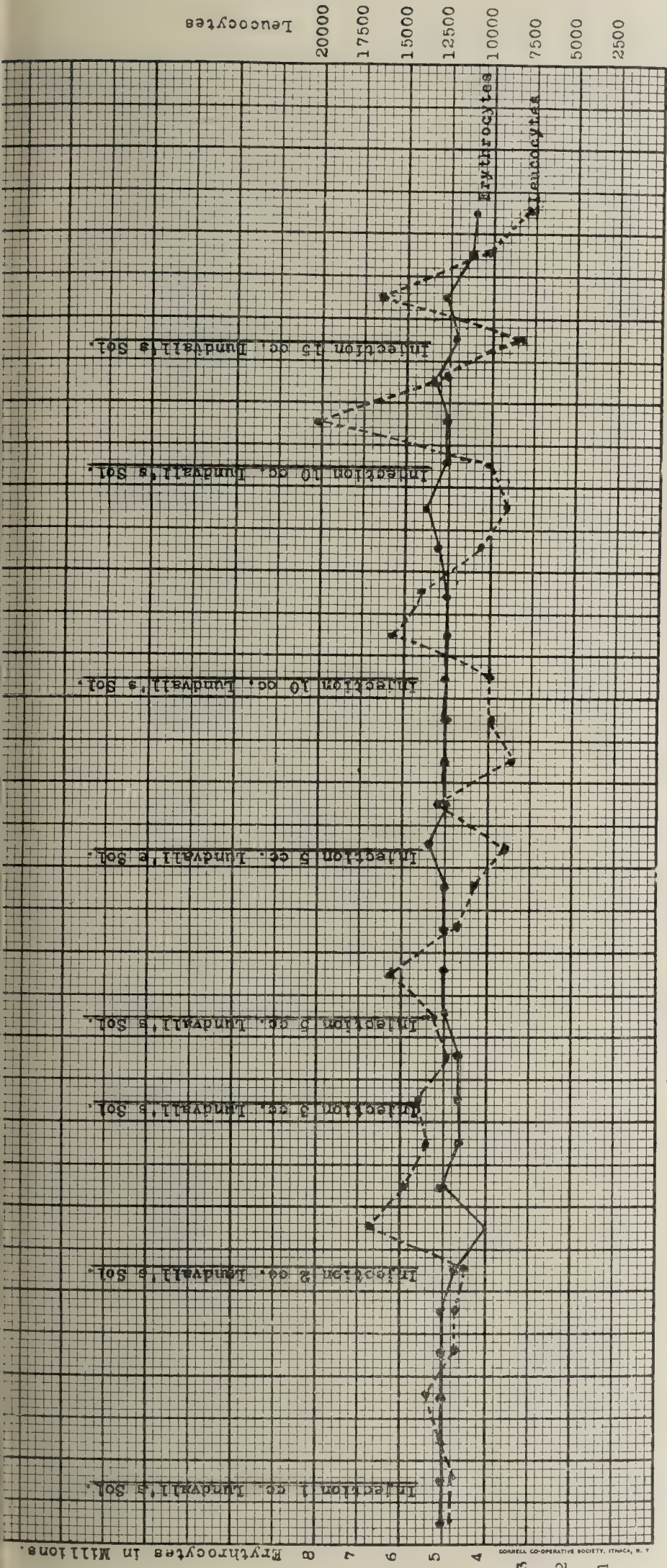
Having thus gained some experience with the action of the solution, we next decided to apply it to the treatment of patients. We selected four patients, one of whom, Mr. S., represented a depressive paranoid reaction type; one Miss T., a hysterical reaction type with schizophrenic features; one, Miss Z., an undoubted schizophrenic reaction type, and the last, Miss F., a depressive reaction type with marked schizophrenic features.

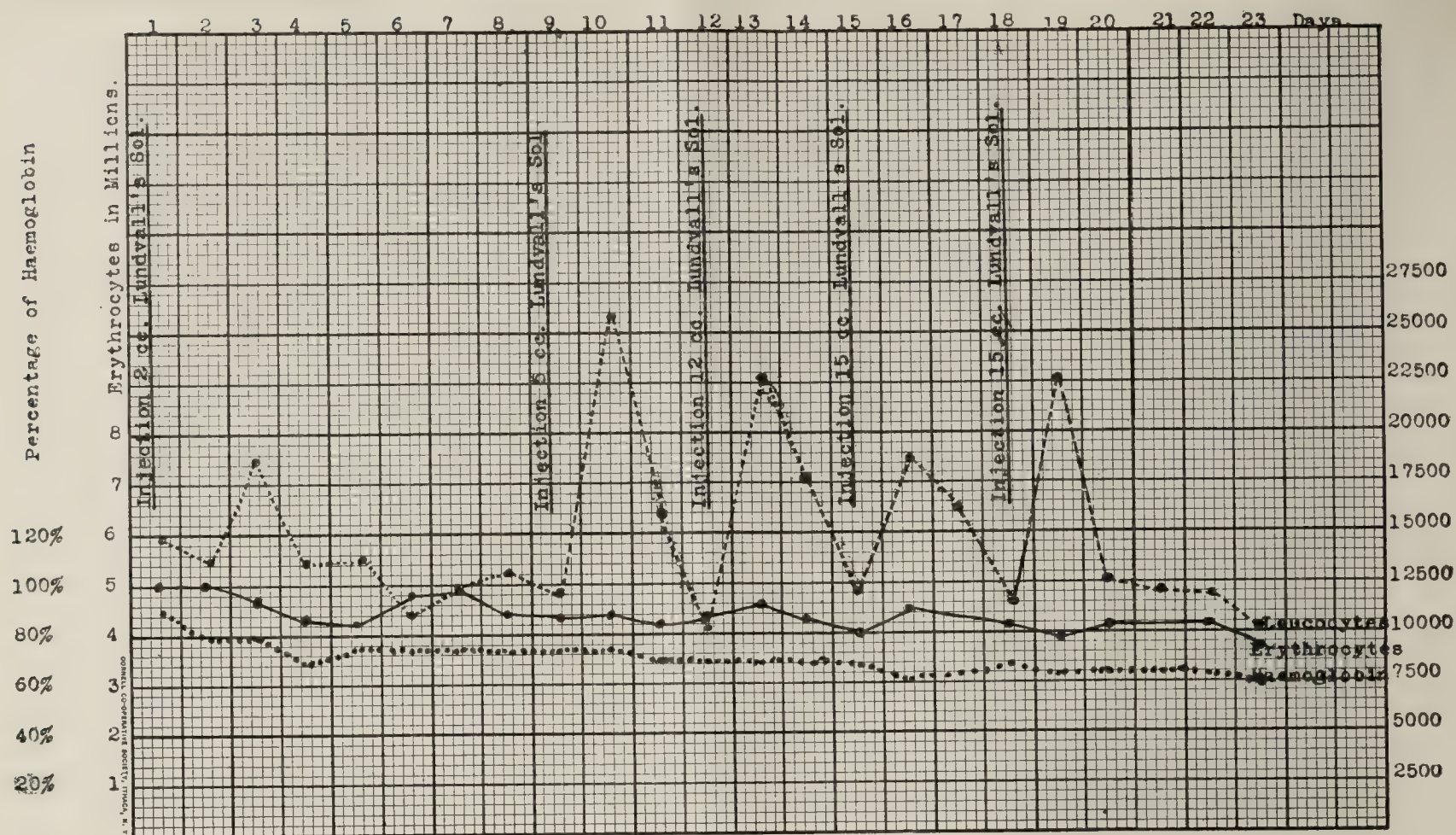
Curves Nos. 3, 4, 5 and 6 will best illustrate the results obtained in regard to leucocytosis, percentage of hæmoglobin, and the number of erythrocytes. Three main facts stand out: The comparatively short time that the leucocytosis lasts, the gradual increase in doses necessary to produce leucocytosis as the patient develops a tolerance for the drugs, and the decrease in the percentage of hæmoglobin and in the number of erythrocytes. The hæmoglobin curve was not plotted in the case of Mr. S. (Curve No. 3). In this case, also, the hæmoglobin decreased from 95 per cent before the treatments were begun to 85 per cent after the last treatment. The decrease in the percentage of hæmoglobin became truly alarming in the cases of Miss T. and Miss Z. (Curves Nos. 4 and 5) reaching as low as 65 per cent in both cases. We were indeed glad to see these patients regain normal blood pictures after the injections of Lundvall's solution had been stopped and iron and arsenic administered in their stead. The differential counts showed the relative increase of polymorphs and the eosinophiles mentioned above. No pathological elements were observed.

As to the psychic behavior of the patients, we can best characterize it as similar to that which one would expect after any shock. The injections are very painful. The rise in temperature of from two to three degrees causes a feeling of being ill at ease, with headache and nausea as accompanying factors, and the whole procedure, necessarily carried on in spite of the protests of the patient, is a cause for excitement. As a result of this shock the patients transfer their attention to the difficulties caused by the treatment and place their own internal difficulties more in the background. Thus, the three schizophrenics who showed a catatonic tendency, were more inclined to talk, and were generally brighter during the twenty-four hours directly following a treatment, whereas Mr. S. the depression case, whose worries were centered on the imaginary prospect of being put in jail and castrated, now worried about the time of the next treatment.

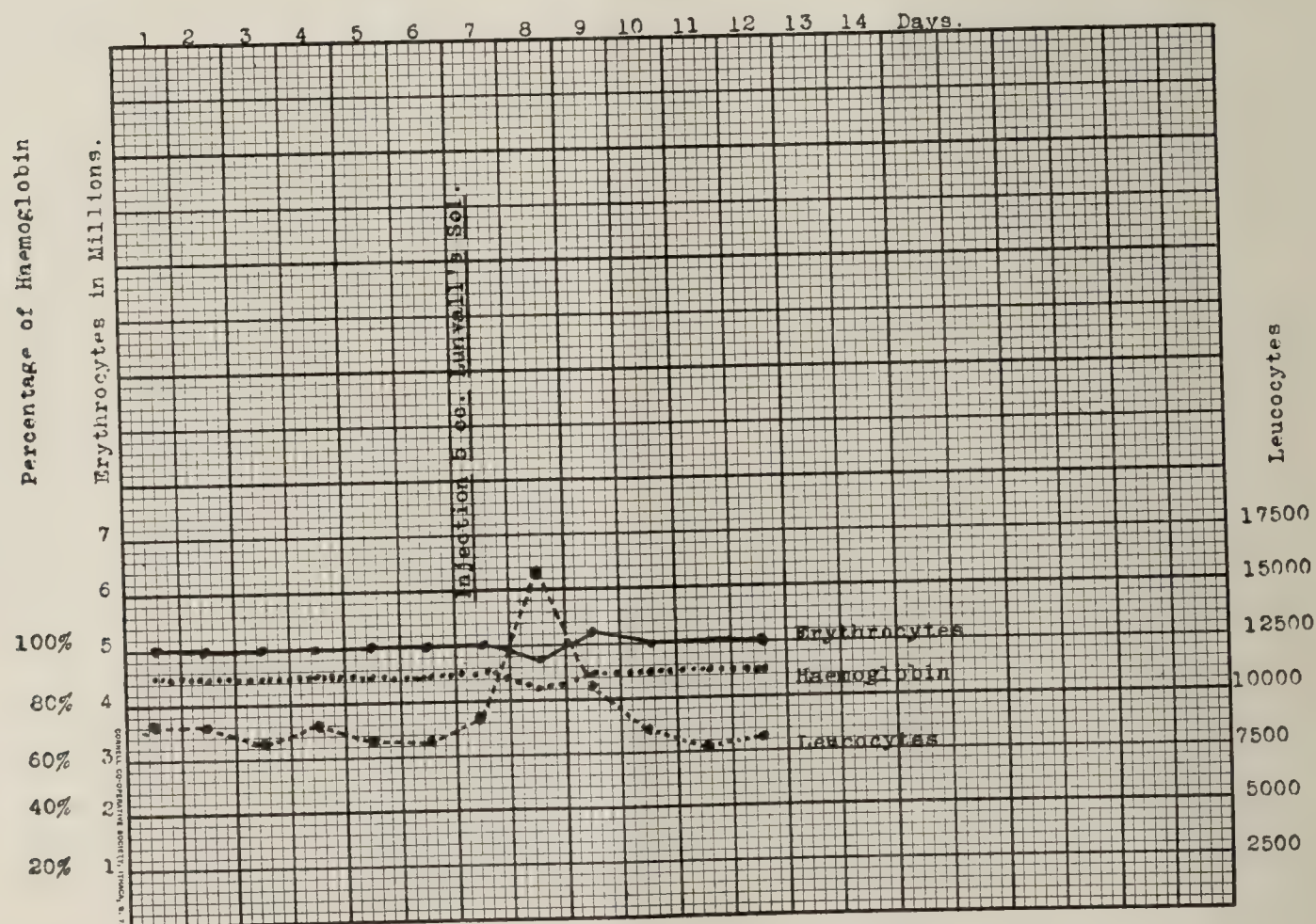
On account of the marked decrease in the percentage of hæmoglobin in two of our patients and the less marked though







CURVE No. 5.—Miss Z. Schizophrenic Reaction Type.



CURVE No. 6.—Miss F. Depressive Reaction Type with Schizophrenic Features.

apparent decrease of this substance in the other two, and in all our experimental animals, we did not feel justified in continuing the treatments. Though the patients quickly regain their original number of erythrocytes, it takes several weeks for the percentage of hæmoglobin to reach the normal figure. These disadvantages would in themselves seem to preclude the continued regular injection of the solution.

SUMMARY.

1. The injection of Lundvall's solution causes an increase in the number of leucocytes.
2. This leucocytosis lasts from one to two days.
3. The patient develops a tolerance for the solution.

4. The hæmoglobin decreases alarmingly if the treatments are repeated at close intervals.

REFERENCES.

1. A good summary of the work done can be found in Merck's Annual Report, 1913, XXVII, 1.
2. Deutsche med. Wchnschr., 1904, XXX, 227.
3. Hygiea, 1907 LXIX, 1142: Tidsskrift for Nordisk Retsmedicin oz Psykiatri, 1910, X, 227. Lundvall: Sonderbroschure, Christiania, 1912.
4. Bayard Holmes: The Insanity of Youth and Other Essays, Cincinnati, 1915, pp. 19 and 195.
5. Busse: Arch. für Gynäk., 1906, LXXXV, 1.
6. Landerer: Deutsche med. Wchnschr., 1893, XIX, 204.

LEUKEMIA, PSEUDOLEUKEMIA AND HODGKIN'S DISEASE.*

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AND

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The diseases which have as their most prominent feature a progressive enlargement of the lymph nodes form a group which offers many difficulties in differential diagnosis. These difficulties beset not only the clinician but also the pathologist. In fact, it may be said that, if the ordinary form of glandular tuberculosis be excluded, there is left a group of diseases which have so many common factors that separation into its component members is only a matter of opinion. This has led to a variety of attempts at classification with results acceptable, as a rule, only to the originators.

The common factors in these diseases, as we have observed them, are in brief as follows:

1. The presence (or history) of a primary focal inflammatory lesion, usually but not necessarily in the upper part of the digestive or of the respiratory tract (teeth, tonsils, adenoid tissue, sinuses, bronchi).
2. Progressive enlargement of the lymph nodes, with or without accessory extranodal tumors.
3. Chronic course, with late moderate secondary anæmia and with the constant development of a fever usually of an irregularly intermittent character, exceptionally of the Murchison type.
4. Eventual fatal termination within a relatively brief period of years (2-5).
5. The occurrence during the course of the disease of either the blood picture described by Bunting¹ as the primary blood picture of Hodgkin's disease, or of a leukemic blood picture.
6. The occurrence of a primary lesion in the germinal centers leading to an early loss of architecture in the lymph nodes through an extensive proliferation of diverse cells but with common factors in the picture.

7. The constant occurrence in the lesions (nodal and extranodal) of organisms of the diphtheroid type.

The group possessing these common features includes the diseases ordinarily designated as Hodgkin's disease (lymphogranulomatosis), leukemia of the lymphatic type, pseudoleukemia, lymphosarcoma, malignant lymphoma, chloroma, leukosarcoma, etc., showing a nomenclature as varied as the classifications. One's first reaction after coming in contact with various members of the group is to wonder whether the same effort that has been applied to the separation of the members of the group, if it had been applied in an attempt to bring them together, would not have increased our understanding of them. In other words, are not their resemblances greater than their differences?

In general the blood picture is held sufficient to separate one group of these cases as specific diseases under the name, "leukemia." This does not seem to us justifiable. The evidence from our series of cases, even though they be few, seems to indicate that the leukemic blood picture is an incidental feature in the course of the disease, or rather an individual reaction to a stimulus which in another case may fail to produce the same reaction. It seems impossible to tell clinically whether or not a patient has a leukemic blood picture. Pseudoleukemia and leukemia are indistinguishable without a blood examination. This was apparent to us in a case recently published in which the cultural findings² were emphasized—a case apparently the counterpart of that published by Wende.³ With all the clinical signs of leukemia, the patient showed the Hodgkin's blood picture until his departure from observation during the last weeks of his life. Owing to this departure we are unable to say whether, as in Wende's case, a terminal leukemic picture was developed.

* A paper presented before the Association of Am. Physicians, May, 1916.

¹ Bull. Johns Hopkins Hosp., 1914, XXV, 173.

² Bunting and Yates: Bull. Johns Hopkins Hosp., 1915, XXVI, 376.

³ Amer. Jour. Med. Sci., 1901, CXXII, 836.

In three cases of so-called pseudoleukemia we have seen the Hodgkin's blood picture persisting for months and in one case for years. In a fourth case, seen by the courtesy of Dr. Warfield at the Milwaukee County Hospital, the Hodgkin's blood picture was succeeded before the patient's death by the picture of acute lymphoblastic leukemia.

The occurrence of a leukemic picture in Hodgkin's disease is apparently relatively rare. However, in one case sufficiently under our control so that all data necessary for accurate diagnosis were obtainable, there occurred a change of the blood picture from the secondary polymorphonuclear leukocytosis of the intense type of the disease to a leukemic picture. With a count of 72,000 leukocytes 65 per cent were of the mononuclear type, both large and small, but atypical and immature. Some of the cells showed mitotic figures. The occurrence in the blood-smear of megalokaryocytes suggested that this represented a bone-marrow reaction. The picture later reverted to its original type shortly before the death of the patient, who showed at the post-mortem examination the lesions of acute Hodgkin's disease. In two other cases diagnosed clinically as Hodgkin's disease (and in one confirmed by the excision of a gland) there appeared in blood-smears submitted to us the formula of chronic lymphocytic leukemia but without apparent marked leukocytosis. We have observed also in a monkey, inoculated with diphtheroid bacilli, the occurrence of a similar picture (99 per cent lymphocytic forms, 1 per cent polymorphonuclear) without any apparent increase in the number of the leukocytes. In another human case, one of acute lymphoblastic (or possibly myeloblastic) leukemia, we have seen the picture of acute leukemia develop through the Hodgkin's blood picture.

Moreover, we find that it is equally as difficult to tell, from the pathological study of the lymph glands in this group of diseases, whether or not the patient had a leukemic blood picture. The glands in a case of malignant lymphoma are identical in appearance with those in chronic lymphocytic leukemia. There is no difference between the infiltrations in the large-celled acute leukemic picture and those in lymphosarcoma or pseudoleukemia. In each case one finds, with an increase in size, a loss of glandular architecture and a diffuse infiltration with the type of cells chiefly involved. It is with such observations in mind that the leukemic blood picture seems to us of incidental importance in the disease in which it occurs.

Pathological study of the glands in these cases shows, as we have just suggested, that in each there is a progressive increase in size, with early loss of architecture. The increase in size is due to a general proliferation of cells which show to a certain extent diverse types. Recognizing the common factors we may, nevertheless, make three broad groupings of the cases even at the risk of earning the censure passed on others who have attempted to classify the group.

In the first class, that of Hodgkin's disease proper, one recognizes a lesion in which destruction of lymphocytes is dominant, but in which proliferation of fibroblasts and of the reticulo-endothelial cells is prominent. This proliferation is

atypical, leading to giant-cell formation. One may recognize three terminal pictures in this group.

1. Almost complete sclerosis (typical fibroblastic proliferation).
2. Sarcomatoid picture (atypical fibroblastic proliferation).
3. Endotheliomatoid picture (atypical endothelial proliferation, usually with marked giant-cell formation).

The last two have the local histological picture of malignancy but without invasion (or only slight) and without any tendency to metastasis or recurrence.

In the second main group of cases we find a large-celled proliferation infiltrating the whole gland. This apparently begins with a marked proliferation of the large cells of the germinal centers, a proliferation which is atypical and which fails also to show the differentiation into lymphocytes. In very early cases there may be a thin collar of lymphocytes about these extremely large germinal centers. In cases slightly later, there are architectural indications of very large germinal centers but no lymphocytes, and ultimately there is a general infiltration of the gland with these large cells and obliteration of the normal architecture. There may be some fibroblastic proliferation, and giant cells may be found. From the character of the predominant cell this might be termed the lymphoblastic group.

In the third group there is a diffuse proliferation of the small lymphocyte with very early loss of architectural landmarks. Scattered lymphoblasts and atypical endothelioid cells may occur. This may be spoken of as the lymphocytic group.

While we make thus pathological distinctions between broad groups, they are not always clear-cut. The fibroblastic proliferation and giant-cell formation may be so marked in the latter groups that a transition picture toward that of Hodgkin's disease is seen. In fact we have no desire to separate the groups but rather would consider them as representing a varied reaction to the same or to similar stimuli. Were it not for the rapid course of acute leukemia (both myeloblastic and lymphoblastic) we should be inclined to see in these cases examples of the general pathological law, that a toxin stimulates in mild doses (lymphoblastic and lymphocytic groups) but in strong doses destroys (Hodgkin's disease).

The above discussion embodies the conclusions at which we had arrived even before we had found that with careful technique diphtheroid organisms could be obtained from the glands in all of these conditions. This finding has been very abundantly confirmed by the work of others. There seems to be no question as to the constant occurrence of the organisms, but only a question as to the significance to be attached to their presence in the lesions. The majority of investigators have concluded that the organisms occurs in too diverse conditions to be of etiological importance.

While we can ask only for a Scotch verdict at the present time, evidence which points toward their etiological significance from our experience is in outline as follows:

1. The constant occurrence of the organisms in Hodgkin's disease and in the allied group under discussion. This is true not only for single determinations but for repeated examina-

tions, as, for example, seven successful cultures from one case over a period of five years (neck, groin and axilla).

2. The occurrence of the organism where it would explain the lesion. We may cite, as examples, its occurrence, as reported, in the cutaneous nodules in a case of acute pseudo-leukemia; and the occurrence of the diphtheroid as the only stainable organism below the surface and distributed in mucosa and submucosa in two cases of primary intestinal Hodgkin's disease.

3. The occurrence of the so-called Hodgkin's blood picture in the whole group of cases enumerated, in laboratory animals (monkey, rabbit) inoculated with the living organism, and in one normal individual inoculated with the dead organisms (vaccine).

4. The occurrence of abscesses in laboratory animals (monkey, dog, rabbit, guinea-pig, horse) at the portal of inoculation with lymph-gland changes similar to those seen in early Hodgkin's disease.

5. The occurrence of complement deviation by the use of the patient's serum and diphtheroid organisms (unpublished series of experiments by Yates and Kristjanson).

6. The occurrence of a glandular reaction and of a skin reaction in patients injected with immune serum resulting from the use of a diphtheroid antigen.

Such evidence we believe would be accepted as indicating etiological significance for almost any organism except members of the diphtheroid group. It is accepted for organisms almost as widely distributed as the diphtheroids. We must admit that the final test, the production of a disease in animals comparable to the human type, has not been accomplished. The attempt to produce a chronic disease in animals less susceptible than man (in whom the virulence is not great in the majority of cases) has resulted usually in lowering the resistance of the animal to organisms more acutely fatal. However, even here death has not occurred before the regional lymph glands have developed definite changes similar to those shown early in the group of diseases under discussion.

This question, however, must apparently be temporarily unanswered without, however, disturbing in the main our contention as to the general relationship of the diseases discussed.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

NOVEMBER 6, 1916.

The Recent Epidemic of Infantile Paralysis. DR. HAVEN EMERSON, New York City.

See article in this number.

NOVEMBER 20, 1916.

1. Exhibition of Patient With a Calcified Cyst in the Right Pleural Cavity. DR. G. J. HEUER.

The patient, a colored man fifty-three years of age, entered the hospital in the service of Dr. Janeway, October 12, 1916. He complained of cough, shortness of breath and pain in the right side. In his past history the only points of interest are the occurrence of typhoid fever and of pneumonia thirty-two years ago. The pneumonia, he states, was upon the left side. His first wife died of tuberculosis at the age of thirty-eight.

Present Illness.—Four weeks before admission to the hospital, while lifting a 300-pound sack of fertilizer, the patient had a sudden severe pain in the right side, accompanied by cough and shortness of breath. The symptoms were so marked that he was compelled to stop work, but was able to walk to a doctor's office. The physician advised him to remain in bed. During four weeks in bed the pain has persisted unchanged. The cough has continued.

Physical Examination.—The physical signs were those of fluid at the right base, which was thought to be purulent in character. A needle was inserted into the chest, but met with firm resistance. No attempt was made to insert the needle farther, and no fluid was obtained.

X-rays of the patient's chest showed a remarkable condition. In the right side of the thorax was a clearly defined shadow, roughly pyramidal in shape, the apex directed upward, the base resting in part upon the diaphragm. This shadow measured 13 cm. in vertical height, was 10 cm. wide. An X-ray taken with the patient in an upright position showed this cystic structure to contain fluid which presented a definite level about 3 cm. from the very tip of

the mass. The clearly defined wall of the structure measured 5 mm. in thickness. The mesial surface of the mass was in contact with the mediastinum. The lateral surface came almost to the rib margin.

Sputum examination was constantly negative for tubercle bacilli. It was purulent in character and contained large numbers of cholesterol crystals, pus cells, and epithelial cells. The amount of sputum varied, some mornings amounting to a cupful.

The temperature was slightly elevated, rising to 99° and 100° during the day. The leucocytes were 7000, the red cells, 3,500,000, hemoglobin, 60 per cent. The polymorphonuclear cells were not increased. There was no eosinophilia. The Wassermann test was negative.

A positive diagnosis could not be made. Various possibilities, such as calcified dermoid cyst, echinococcus cyst, an old circumscribed empyema associated with calcification, and a localized hematoma associated with calcification, were considered.

Operation.—About twelve inches of the ninth rib were resected, and later, about six inches of the eighth rib. The parietal pleura was stripped from the chest wall. Palpation of the pleura showed directly underneath it a hard, bony mass, the limits of which could not at first be determined. On incising the parietal pleura, what appeared to be the bony wall of the structure was found densely adherent to it. The dense adhesions were cut, and the enucleation of the calcified mass begun. It was found that over the entire anterolateral surface of the mass there were these dense adhesions between it and the pleura. The flattened surface of the mass in contact with the diaphragm was much less adherent and could be readily separated from this structure. The deeper surface of the mass was in contact with the concave surface of the lower lobe of the lung; it was not at all adherent and could be readily separated from it. The mesial aspect of the mass was densely adherent along the anterior mediastinum. During the course of the removal of the tumor, the cyst wall along its mediastinal border was entered. There was an escape of a thin, yellowish, purulent material, and some bubbles of air. At the upper lateral border of the mass, where the calcareous wall apparently had not been penetrated, there was again an escape of

fluid and air bubbles, and it was assumed that here there was a communication between the cyst cavity and the lung. The entire mass was finally removed without hemorrhage, without, indeed, tying a single blood vessel. It was noted after the removal of the tumor that the visceral pleura of the concave lower surface of the lung was not thickened. The large cavity left after the removal of the mass was drained with a single rubber tube.

There were no post-operative complications. The patient is well two months after operation.

Examination of Specimen.—The calcareous wall is complete, with the exception of one area along the mesial aspect of the tumor, where the mass was densely adherent to the mediastinum. The wall varies from 2 to 5 mm. in thickness. At the time of removal, the interior of the shell was lined with a putty-like dirty brown deposit, which could easily be scraped off from the wall of the cyst. This material on examination showed nothing excepting cellular detritus. The cyst contents were very thoroughly studied by Dr. Guthrie, without anything being found to establish the nature of the cyst. Sections of the cyst wall showed calcified tissue. In no place was true bone found.

2. Medical Problems of the War. DR. W. H. WELCH. (Abstract.)

There would not be time to attempt the treatment of any such broad subject as the title would indicate. What I shall have to say will relate to some of the medical problems of the war, and more particularly to my own personal experiences. That necessitates saying a few words as to the circumstances of my making the trip to England and France last August and September.

I went over primarily to make some inquiries and observations which I thought might be helpful in planning and organizing the new School of Hygiene and Public Health which is to be established here. I wanted to talk over some of our problems, but it was very difficult to arrest the attention of anybody over there on anything except the problem of the war. I was also interested in the qualifications of certain young men for taking up some of the work here. It soon became perfectly apparent that no one is coming over here while the war is on. In the first place it is difficult to get hold of them, and they were so intensely absorbed in their work it was difficult to divert their attention. I soon made up my mind that any men willing to come here while the war is on would doubtless be the type of men we would not want. Their duty is there with their country.

The second purpose of the trip related to a commission that the President of the United States has placed upon the National Academy of Science, and I was accompanied by Mr. George Hale, the eminent astronomer, who is head of the solar observatory at Mt. Wilson, California, which is supported by the Carnegie Institution. He has been engaged since last March in undertaking this work for the organization of the scientific resources of the country in questions of national security and national defence. It is obvious to anyone that it would be most helpful to learn what they are doing on the other side in those directions stimulated by the war. The opportunity of meeting members of the government and eminent scientific men was intensely interesting, but that is a subject by itself, although it occupied a considerable part of our time.

When I went over I did not plan to go to France, and did not suppose that I should have the opportunity of seeing very much of the actual medical and surgical work. Fortunately, I had had France included in my passport, so it was possible to go there. I might say here that I was not aware of the importance of taking with one all the credentials one should have. I went in rather a casual way with an ordinary passport, and gave our embassy both in London and Paris a very unnecessary amount of trouble, which would have been avoided had I taken letters from our ambassador and others.

One should not think of going over there simply because he wants to go to see things. One must have a serious purpose before going. Indeed, one is not likely to get a passport unless he has a serious errand, and unless he has, he should not be there. In a way it is almost like going to a house of mourning without being called by a purpose.

We left the United States on the 5th of August and went over on an American steamer, landing at Liverpool. I came back on an English boat, the *Baltic*, and the contrast was interesting. Apparently, everyone wishes to go on the American boats on account of the security. On that boat everything was done to make our presence widely known. We advertised ourselves all the way across. An American flag was painted on the outside of the boat, which was brightly illuminated at night. We went up like a banner of flame through the Irish Channel. That is, of course, a matter of safeguard. Coming back, on the other hand, everything was done to conceal our presence. There were no lights at all and the decks were perfectly dark at night. We did not know where we were. There was no record posted of our daily run, nor of the latitude or longitude. The course that we took was not known, except perhaps to the captain of the boat whose orders were handed to him at Liverpool.

On landing we went to London where we had our headquarters, making several side trips, especially to Oxford, where I went three times to see Dr. Osler. I also went to Cambridge and a few other places. We crossed the Channel at the end of August from Southampton to Havre, and visited Paris. Although the trip to France was hurried, lasting only about two weeks, we had rather exceptional opportunities for seeing things in Paris, in the American hospital at Neuilly, at Compiègne, etc. When it was time to go back, we found we were held up in Paris on account of a sudden taking off of the boats crossing the Channel. Mr. Hale took a French boat home from Bordeaux. I remained nearly a week longer before the boats started again from Havre to Southampton.

On the whole I think I saw about as much as one could see in that short space of time. I owe that very largely to Dr. Osler. I would like to say in passing that both Sir William and Lady Osler were really very well and very active indeed in work of all sorts relating to the war. I thought Dr. Osler was in extremely good form, intensely interesting and interested, and a very great influence over there. He has done important things of real national service to us over here, particularly those of the medical profession. For some reason or other it was a long time before we had any medical men over there observing the military medicine and surgery. Why, I do not know, but they were not there. Dr. Osler interested himself and wrote to the President here and to others, and through his interest and activities it was arranged that a group of very excellent young doctors from our Army and Navy Medical Corps should go over to take advantage of the opportunities for important observation. Dr. Osler introduced me to Sir Alfred Keogh, the Director General of the Army Medical Corps and head of all things medical, who opened the way everywhere, both in Great Britain and France, and afforded me exceptional opportunities of seeing things and of meeting men I desired to meet. When Dr. Carrel heard I was in Paris he spent nearly two days there while the Minister of War was making arrangements for me to go to his hospital. Everything requires time and there are many formalities. Things are not quickly attended to.

Now a few words on some of the broad aspects. In the first place the conditions under which the warfare is conducted are perfectly unparalleled. Of course, there is a large experience from past wars of military surgery, hygiene and organization of hospitals, etc. This is valuable and all important. I do not think that they utilize sufficiently some of the experiences in our Civil War, but the problems are to a large extent novel because the conditions are new. If you read of military surgery, you will note it is based largely upon the assumption that in warfare bullets from small

caliber guns fired with great velocity are to be used; whereas, in the present war the wounds are terribly lacerated and often contain broken shrapnel. One shell may burst into thousands of fragments raining down upon the men. You can imagine what novel conditions result from that. Poisonous gas, too, is a terrible thing which was never heard of before. Warfare in the trenches is new also, and there the men are subjected to new conditions of infection. I heard a most vivid description of the environment of the soldiers in the front line trenches from Dr. John McCrae, who is over there in a Canadian hospital. He told of the shells shrieking with no let up by day or night, the shrapnel bursting into these myriads of fragments and the killed and wounded everywhere. No wonder there are effects upon the personality and nervous system which are absolutely new and which one has had no experience with before.

Again, by way of a general statement, we are in possession of weapons of defense which have not been tried on any such a scale before against the diseases and wounds of the war. Here was an opportunity to test the value of our inoculations against typhoid, paratyphoid, cholera, dysentery and tetanus. It is a wonderful chance to see what these new discoveries are worth and to try them out. There has also been a great opportunity in sanitary matters and the possibility of having pure water, new methods of incineration, etc., and the sanitation of camps, which has not been in the possession of military men before. Broadly stated, there are certain things which stand out with great prominence in regard to sanitation and preventive medicine in this war. The diseases which have been so devastating in past wars are to a large extent controlled. This is probably the first war where the soldiers have died to a greater extent from wounds inflicted by bullets and shells than from disease. The control of disease is one of the great lessons of the war. Typhoid and paratyphoid *a* and *b* were not unknown in the earlier part of the war, but are now controlled by vaccination with killed cultures of the bacilli. Typhoid and paratyphoid vaccines are given in one dose, one vaccine, and I believe that on the Eastern front, where there was some cholera, they included the cholera vaccine at the same time. I believe it is possible to use the Shiga bacillus in one vaccine with the germs of a great variety of diseases. When we recall the terrible mortality from typhoid fever in our Spanish-American War, you can see what a tremendous gain this is.

Equally significant is the control of tetanus. Early in the war, when there was not enough serum, it was obvious that there was going to be a great deal of tetanus. It is now practically under control.

Cerebrospinal fever is quite satisfactorily treated at present. Their results at first were very unsatisfactory, when it was found that they were using a practically inert antimeningitic serum both in Great Britain and France. They had not known it and the treatment of Dr. Flexner threatened to become discredited. He obtained some of the serum to test and it was found to be worthless, which has led to the examination of not a few of the commercial antimeningitic sera. The armies are now being supplied with a really good serum, largely through the agency of the Rockefeller Institute, and the results are extremely satisfactory.

In the East they have had diseases which have not prevailed much in the West. Dysentery has occurred on the Western front, but has prevailed chiefly in the East.

Just a word about tuberculosis, which is one of the medical problems of the war. The situation as regards that disease is really a very serious one in France. It does not appear to be so in England, and probably is not in Germany. We do not, of course, have any information as to what the situation may be there. In France there is a frightful amount of tuberculosis among the soldiers. To a very large extent, those who have been temporarily disabled are found to be tuberculous. It raises the question as to what the explanation may be. Probably tuberculosis is more common in

France than in Great Britain or Germany, so there are larger numbers of soldiers with latent tuberculosis. In the second place, it is probable that not sufficient care was taken in the examination of the recruits, so as to exclude those with active and especially open tuberculosis. Then, too, France has been behind the other countries in the tuberculosis movement, and they have not had the lessons in protection, especially the importance of the open air life.

I might say that in general the soldier's life is a healthy one. Take the British Tommies, for example. The British workingmen and clerks have been trained into admirable soldiers, and you would hardly recognize them as the class that some have represented as a rather degenerate type. No praise is too high for the British soldier. The men are healthier than they were before and probably tuberculosis, instead of being on the increase, is controlled. This is not so, however, among the French. It is a really serious and urgent problem, which is causing great concern over there.

The results obtained by the surgeons are most remarkable. I feel that important contributions have been made, and are being made, toward the treatment of wounds. The use of the X-ray is, of course, of incalculable advantage. This is obviously the case when you consider the rôle the lodgment of foreign bodies in wounds must play.

A word as to the sanitation of camps. I regret that I did not personally visit one of the camps near the front. Sir Alfred Keogh was anxious for me to go and had arranged for it, but I had to hurry back and so missed the opportunity. I made up for it to some extent in London when I returned and went to see the field experiments which are being made. That is something which is not shown very generally, I think; at least our doctors over there in connection with the embassies had not seen these places. I was taken to a large open field, fenced all around, and there it was most interesting to see the experiments they are making in such matters as purification of water, latrines, disposal of waste, etc. I was most enthusiastic about the incinerators. There is no expense for fuel, as they are going day and night. All waste is dumped there and burned up.

As regards the organization of the hospitals, of course in England they are all the so-called base hospitals of different types. The general organization is this. When a soldier is wounded in the trenches, he may have to wait until dark before he can be safely removed, so that he may have to have first aid there. He is then carried back from the trench to the hospital at the front, where he is looked after more thoroughly and is perhaps operated upon. He may stay there several days if necessary, but the treatment is usually temporary, and he is sent back from this front hospital to the casualty clearing station, where his destination—whether he shall be sent to a base or a semi-base hospital—is determined. There he also may remain and be treated a third time, if he is an emergency case. He is then sent to Paris or to the Versailles region, or if he is in British territory, to one of the hospitals around Boulogne. The distribution to the individual hospital is determined by distributing officers. The active operating centers are not, strictly speaking, the base hospitals. The American Ambulance controls about 2000 beds, but less than 600 are in the actual operating center. Where Dr. Blake is (Hospital No. 76 in the Versailles region) they have 250 beds in the active hospital, which occupies a large school building and is very well adapted to the purpose. From there the patients are moved on as soon as they can be to the outlying dependent hospitals or convalescent homes. The experiences of the individual hospitals may be very different according to the class they belong to. Thus, we have the casualty clearing station with one kind of experience, and then the semi-base hospitals that see a different class of wounds or diseases; and still more different the patients in England, who have been carried across the Channel to genuine base

hospitals, which are quite different from the hospitals nearer the front. Then there are hospitals of various special sorts. A very great problem, to which they are already beginning to turn their attention, is the future of the disabled soldier. You can imagine what a tremendous problem that is. They are beginning to establish institutions for the industrial training of these men. Such is the work that Miss Winifred Holt has been doing for the blind in Paris.

The first friend I met after my arrival in London was Dr. Adami, who is in London in charge of very important statistical work, looking after the records of the Canadian soldiers. A great deal is done to make sure that the records are available for statistical study and analysis, and for the history of the war later. The British Army has a very excellent statistician, who is in charge of it all. After the war they will have the benefit of all that systematic work as regards history taking, etc. Dr. Osler appeared the next morning and said that was his day for visiting the heart hospital at West Hampstead. He visits different hospitals at different times. They have established special hospitals for the observation of different classes of disease or injuries. This one was for the reception of patients with the so-called "soldier's heart." At the Maudesley Hospital all the cases of neurasthenia, and especially the shell shock cases, are received. This is no new thing, but is one of the contributions of our Civil War. One of the best things done in our Civil War was the establishment of these special hospitals, especially that notable one in Philadelphia for nervous injuries, to which Drs. Keen and Weir Mitchell were sent, and where Weir Mitchell did that memorable work that turned his attention to the field of neurasthenic disorders. The working up of heart cases is another contribution of our Civil War, particularly of Dr. Da Costa—that particular group of cases where there is insufficiency of the heart attributed to the terrible strain of forced marches, etc. The cases in the West Hampstead Hospital are in that group. You can imagine how interesting it is to have the opportunity of studying them by the newer methods, the electrocardiograph, etc. Perhaps some of you have seen some of the discussions about it. There was one before the Royal Society of Medicine by Mackenzie. If so, you know, more or less, the points of view. Perhaps the most important point is that the majority of these cases apparently give a history of damage to the heart before they were enlisted. They have a history of rheumatism, or breathlessness on going up stairs or on exertion. In other words, they did not have perfectly normal hearts and they could not stand any really great physical strain. In fact, some think these terms are misnomers, and that it is merely the fact that the condition under which they live has unmasked the disorder which was already there. That is probably taking an extreme view.

Another hospital I visited with Dr. Osler was the Canadian Hospital at Cliveden. We motored over one beautiful day from Oxford to that charming place where Major Astor lives and where they have had this fine hospital constructed. It is of the barrack type of military construction, which again is a contribution from our Civil War. This used to be called the American system of hospital construction. I did not know of it until I went to Germany the first time, when I saw a hospital at Leipzig which they called "built on the American system," and I found that it was on the barrack plan of construction. At Cliveden various classes of patients are received, both the wounded and patients with diseases. There I first visited a ward given up to patients with the so-called trench nephritis. The word "trench" is applied to all sorts of disorders and diseases which are not clear as to their causation. It is often a misnomer, as the conditions occur in men who have not been inside the trenches, but you hear of trench fever, of trench foot, of trench shin, trench nephritis, etc. This nephritis was first recognized as a disease occurring in camps among the soldiers in our Civil War. Dr. Osler spoke to me about it and said it was quite well described as one of the camp diseases, so it is

not new. There is a great deal of interest attaching to it. I saw one ward practically filled with patients with albuminuria, dropsy and other evidence of unmistakable nephritis. The question as to the etiology is open and there are various views held. I came across from the other side with Dr. Hugh Cabot, who has been in charge of the Harvard Hospital. He was much interested in this group of cases. He had found the streptococcus in the urine in somewhat similar cases in this country. I might say that a great deal of interest attaches to these streptococcic infections. They told me that the viridans group plays a considerable part, and that by making systematic examinations of the blood, using considerable amounts of blood, the streptococcus is found in surprising frequency and in the most varied groups of cases. This is, of course, interesting and one of the medical problems of the war.

I referred to the Maudesley Hospital, which was not open before the war. This hospital is entirely for the reception of cases of so-called shell shock. I don't think there is any group of cases so pathetic as these. I saw a ward with perhaps 25 soldiers, who were all victims of this terrible condition. They stand up when the physician makes his rounds. Most of them had continuous tremor with staring eyes, a look of terror and blue, cold extremities. When examined, they show various manifestations which we are not apt to attribute to hysteria. Some are deaf and dumb and some are dumb. The disorders of the special senses are most remarkable. The condition is described under various names, such as shell psychasthenia or shell neurasthenia, but it is commonly called shell shock. So far as one can judge, they look on the whole to be rather inferior types both physically and mentally. I was told they were of the type that cannot stand alcohol and were total abstainers in about 80% of the cases. Two of the patients had never been wounded. There has been a good deal of discussion as to how many of the patients may be malingerers, and this has to be considered most carefully. There is no doubt an element of malingering in some of them, but it is impossible that the greater majority of them should be of this type. These conditions are tremendously interesting to the psychologists. I found Dr. Sherrington of Oxford devoting much attention to them. He called them disassociation of special senses. Meyer's view is that they are inhibitions from a tremendous disturbance of the consciousness of the personality of the individual, so that various nervous tracts are blocked for the time being. Some of the patients are treated by hypnotic suggestion with a good deal of success. Dr. Sherrington was telling me of a case in which the patient had been anesthetized and was cured by the anesthesia. Sometimes, when the patients go under the anesthetic, they regain their speech, and sometimes they begin to talk when they are coming out of it. Then they can continue to speak.

Of course, the great problem of the war is the handling and treatment of wounds. I came into contact with that when I reached Paris. The following day I went out to the American Ambulance Hospital at Neuilly. This is an institution of which we should be very proud. Not that we are doing enough, for we are not beginning to do enough along these lines, but it is a splendid institution, splendidly managed, and splendid work is done there. I saw nothing finer. They started at first with the system of changing units. The Harvard unit went there and I think the Chicago unit also. This was a bad system undoubtedly and has been abandoned in the Harvard Hospital, which is to have permanent heads. Obviously it is not a good plan to be constantly having one group of men go and another group replacing them. I understand that Dr. Hugh Cabot is going back as the permanent head of the Harvard Hospital in the district of Boulogne. The American Ambulance is more or less permanent. One side is more or less French, and the rest of the hospital, the more active part, is under Dr. Hutchinson of Philadelphia. He is doing splendid work, and it is a great inspiration to see him. There

is one doctor at the American Ambulance who simply went over to see things, but who became so absorbed he never left. That is the right spirit, and when one considers not only the scientific and professional interest, but the tremendous human interest as well, it is not surprising he stayed. There is a good laboratory there, with one of our younger men as an assistant. It was at the American Ambulance that I learned at first hand, for the first time, of the various methods and ideas regarding wound treatment. The wounds are to a large extent infected by bits of shrapnel or shell. There are some bullet wounds. Some of the types, which Dr. Cushing has described so well, are most interesting, where the men, particularly the Australians, cannot keep their heads down in the trenches, but will look over, and the bullet cuts right across the top of the skull.

I may say there is no conceivable injury which is not inflicted in this war. When I went to Boulogne to visit Sir Almroth Wright, one man said to me: "You must not go without looking at some of my cases. You will never have such a chance again." He showed me a case of Brown-Séquard's paralysis from an injury. One might indeed go through life without seeing a case where just one-half of the spinal cord was cut across. It is a wonder to me that more of those who can go are not over there to acquire some practical experience.

To return to the treatment of wounds. They are nearly all infected. The bacterial flora of the wounds is carefully studied. There, of course, is a wonderful field which is by no means exhausted. The bacillus which we worked with here many years ago, the gas bacillus responsible for gas gangrene, is seen in nearly all of the wounds. The results which are obtained in the treatment of wounds seem to be on the whole fairly good, so far as I could judge. Unquestionably the most brilliant results are those of Carrel at his hospital at Compiègne, an exceedingly interesting hospital about 50 miles out of Paris, with no very heavy fighting going on in front. Verdun is on the east and the Somme on the west. Dr. Carrel is at the end of a salient with great preparations for the reception of wounded. Thousands of men are provided for in that region. Carrel has relatively few cases as compared with the more active hospitals, but his results are surprising. As I understand it, the general principles which guide him, and most of them, are these: First, a very thorough opening up of the wound, with the removal of all foreign material, dead tissue, torn and lacerated tissues, etc. The cleansing of the wound follows and it is that part which takes time. This is done at Carrel's hospital with unusual care and is perhaps better managed there than anywhere else. Then comes the irrigation of the wound. Some think it a matter of indifference as to which irrigating fluid is used, but not so Carrel. His theory is that he is actually sterilizing the wound and the disinfectant which he uses is Dakin's solution, which has been modified to some extent by the use of bicarbonate of soda to render it less irritating. There is nothing new, of course, about the solution, but this is the prevailing disinfectant. After that there is an ingenious arrangement of small elastic tubes, connected with a single tube, which is attached to an irrigating bottle. These are inserted into the wound. By Carrel's method, it is necessary for the nurse to flood the wound every two hours. Then throughout from the start there is a bacteriological control. The determination of the behavior of the bacteria under the influence of this treatment is made from smears, usually from every part of the wound. At Carrel's laboratory the methods are very thorough. Everything is charted and worked out mathematically. The surgeons determine when the wound can be closed by the disappearance of the bacteria. Carrel spoke of sterile wounds. I suspect that cultures could still be grown, but the wounds are sterile surgically. You will say: "What is new about that?" There is nothing new in any one thing, but I

think there is something new in the thoroughness with which the method is carried out in every step. If you go through Carrel's hospital and see his work, you feel that he is making a perfectly definite contribution, and although you may not accept his theories, you can see that his results are better than those elsewhere. Over there, some of them attribute it to the fact that he gets better cases, perhaps only two or three hours old, whereas in some hospitals the wounds are two or three days old when received. He also has a superior hospital, with the necessary funds. Whatever it may be, he obtains these results, which I think would impress anyone. Sometimes, in from 36 to 48 hours the wounds are all closed up, and they get beautiful clean scars from these bruised, lacerated wounds, so one cannot but feel that Carrel has made a real contribution. Dr. Hutchinson, at the American Ambulance, knew about it and he had made up his mind to introduce the Carrel methods in every detail.

Dr. Blake is at Ris-Orangis, and seems to have very sane views on everything. His great contribution is the treatment of fractures, and his results are very remarkable. I did not see any ward which looked just like his. He has good appliances which looked very ingenious, by which extremities are put into every conceivable position necessary to bring the parts into the right relation with each other. He is always trying out various methods. He told me he thought that one method is better for one stage of the disease and another method for another, and that in changing from one to the other good results are obtained.

One of the most interesting things is the part played by dentists there. At the American Ambulance there are rooms filled with dental chairs. This is a very essential part of the work. Every hospital I saw had some dental work, but none in which it was carried out so wonderfully as at the American Ambulance.

The removal of foreign bodies has become a definite specialty. I heard the other night of one surgeon who does nothing but go around to different hospitals and remove foreign bodies with extraordinary deftness. Most surgeons do not believe in removing foreign bodies, claiming that they do not do any harm. This man has a deftness which is said to be most wizard-like. The foreign body is located by X-ray pictures taken at different angles. He then goes in with extraordinary accuracy. He has a little electric magnet device at the end of his finger, with a telephone attachment to the ear. When he is within a certain distance of the foreign body it registers on the telephone.

There is not time to speak of many interesting and important things, such as trench fever. I hardly believe that this is an ordinary streptococcic infection. It is not typhoid fever, nor paratyphoid fever. It is very probably a new disease, not identical with any we have had before. It is a relapsing fever, and some think it may be conveyed by insects or lice, like typhus.

Surgical shock is a fascinating subject. Dr. Porter, professor of physiology at Harvard, has been living in the trenches studying shell shock. I saw him a few days ago in Boston and asked him to come down here and tell us of his experiences, which he promised to do.

Venereal diseases are a terrible scourge and everybody is quite awake on the subject.

I have occupied more time than I should, but I have only touched upon some of the experiences. I would like to add this. The problems are of intense interest and whatever your particular line may be—surgical, medical, bacteriological or physiological—I am convinced there is some field there which will prove of absorbing interest. If you have an opportunity to go there and avail yourself of this unique experience, you certainly should do so. I think it would be surprising if any surgeon who had the chance did not jump at the opportunity. I would say the same thing to young men who are more interested in the laboratory side of the work or in medical problems.

Dr. Watson: What is the nature of the poisonous gas?

Dr. Welch: I am afraid you will have to ask the Germans that. It is believed to be mainly chlorine. Various kinds have been used, but chlorine, I think, has been most commonly employed. It is regarded still as the worst, although perhaps not the most deadly. I might say that some of the physiologists are directing their attention towards protection against gas poisoning. It is now provided against quite satisfactorily and is not of great consequence any longer.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB.

NOVEMBER 13, 1916.

1. On the Etymology, Popular and Scientific, of the Term for Kidney in Various Languages. DR. D. I. MACHT.
To appear later in the BULLETIN.
2. Prehistoric Pathology—Paleopathology. DR. ARNOLD C. KLEBS.
To appear later in the BULLETIN.

NOTES ON NEW BOOKS.

London, Oxford Medical Publications: *Cerebrospinal Fever*. By THOMAS HORDER, R. A. M. C. Cloth, \$1.25. (Henry Froude and Hodder & Stoughton, 1915.)

Medical Hints. By COL. J. EDWARD SQUIER, R. A. M. C. Cloth, \$1.00. (Henry Froude and Hodder & Stoughton, 1915.)

Abdominal Injuries. By PROF. RUTHERFORD MORISON and LIEUT. COL. W. G. RICHARDSON, R. A. M. C. Cloth, \$1.00. (Henry Froude and Hodder & Stoughton, 1915.)

Wounds in War; Their Treatment and Their Results. By LIEUT. COL. D'ARCY POWER, R. A. M. C. Cloth, \$1.00. (Henry Froude and Hodder & Stoughton, 1915.)

These small Oxford War Primers deserve the attention of civilian medical men who are liable for army service. In his volume on cerebrospinal fever, Horder gives an excellent presentation of this disease as observed by him during the epidemic in England during the first year of the war, with a consideration of the special features presented by the disease among soldiers. The serum treatment is recommended as the most valuable means of combating the epidemic, and emphasis is laid on its early use as well as on the great importance of early isolation and prophylaxis.

In his *Medical Hints* Col. Squier gives some excellent suggestions to the civilian physician who is called to active service. He emphasizes the great care which must be taken in the selection of recruits and careful observation of their training in order to produce an efficient fighting force. Since the true function of the medical officer is the prevention of disease, a large part of the book is taken up with suggestions as to prophylaxis. The efficiency of the troops being absolutely dependent on their marching ability Squier emphasizes the importance of the care of the feet and gives valuable suggestions as to the prevention of trench frost-bite which has made necessary the withdrawal of so many otherwise healthy soldiers.

In *Abdominal Injuries*, Morison and Lieut. Col. Richardson discuss the symptoms and types of abdominal injuries caused by different kinds of projectiles and the indications for operation. They believe that "all abdominal injuries should be operated on, but only in properly equipped hospitals." Owing to the efficiency of the Royal Army Medical Corps they state that the majority of patients can be brought in six hours to a well-equipped hospital where abdominal operations can be undertaken. Of penetrating abdominal injuries 20 per cent are hopeless, but with early operation 60 per cent of the remaining patients should recover. The technique of abdominal operations is discussed but the author's recommendations would find but few advocates among American surgeons. He is in favor of flushing the peritoneal cavity with salt solution and the use of the Murphy button when resection is necessary. No mention is made of the often life-saving measure of enterostomy, either as a primary procedure or in the treatment of post-operative complications.

Lieut. Col. D'Arcy Power in his *Wounds in War* is an advocate of Watson-Cheyne's technique of cauterization with carbolic acid, but states that this treatment is only suitable for wounds seen forty-eight hours after injury. Little emphasis is placed on

Wright's views and the physiologic basis claimed for them, and no mention is made of Dakin's solution. The types of wounds caused by the different projectiles are well discussed, and valuable suggestions made for treatment *en route* to the wounded man's final destination. The author lays special emphasis on free incision for all infected wounds. A whole chapter is given over to the vaccine treatment, but little emphasis is laid on the importance of routine injection of the wounded for the prevention of tetanus. In his brief discussion of this disease the author makes no mention of magnesium sulphate, which has proven of so much value.

I. A. C. C.

Harvey's Views on the Use of the Circulation of the Blood. By DR. JOHN G. CURTIS, M. D. Cloth. (New York: Columbia University Press, 1915.)

This book, which represents Dr. Curtis' translations and his ideas about Harvey, has been published under the editorial supervision of Dr. Frederick S. Lee. In the different chapters are taken up in succession the various points about the circulation in relation to the tissues and respiration, until the author finally works up to the actual demonstration of the return circulation. Perhaps the most interesting chapter is the fourth, in which the first recorded mention of the movement of the blood in a circle is shown in a photograph of the page from Harvey's lecture notes of 1616. Everywhere throughout the text there are splendid translations of Harvey's writings. At the end of the book, there is a long list of notes for reference from the text, which will enable the student to trace out the exact source of information on all the points mentioned.

J. A. C.

Modern Medicine and Some Modern Remedies. By DR. THOMAS BODLEY SCOTT. Cloth, \$1.50. (New York: Paul B. Hoeber, 1916.)

This little book, although written for the general practitioner, is to be recommended to the student, first of all, on account of the interesting preface by Sir Lauder Brunton. Any student that contemplates taking up general practice, and who knows the type of work that is before him, can be helped a great deal by reading this little essay. Dr. Scott writes in a very interesting manner, his introduction laying stress upon the difference between hospital and private practice. The section on the diagnosis and treatment of cardiac disorders is well written. There is an interesting chapter on therapeutic speculations and doubts, in which the functions of the glands of internal secretion, more particularly, and their therapy are considered. On the whole the book is well worth reading.

J. A. C.

NEW PUBLICATIONS.

The following monograph is for sale by The Johns Hopkins Press, Baltimore, Md.:

Relation of Tonsillar and Nasopharyngeal Infections to General and Systemic Disorders. By S. J. CROWE, S. SHELTON WATKINS and ALMA S. ROTHHOLTZ. 63 pages. Price, \$1.25.

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SACRO-ILIAC STRAIN.

By WM. S. BAER, M. D.,

*Associate Professor of Clinical Orthopedic Surgery, The Johns Hopkins University; Assistant Visiting Surgeon,
The Johns Hopkins Hospital.*

Much has been written in recent years, particularly by orthopedic surgeons, concerning sacro-iliac strain. But the subject seems to me to deal with a class of cases which are constantly being seen by the general practitioner—a class of cases which is somewhat puzzling, and yet whose treatment is very simple. Risking triteness, I venture to bring it before you to-day.

We have all, I am sure, been rather wearied, and at times even annoyed—annoyed possibly because of our own ignorance—by patients who present themselves before us complaining of pain—a pain continuous and at times severe—in the small of the back or down the thigh. At times the pain is a simple ache, but at times of such severity that one can neither work nor sleep. We have called it rheumatism, sciatica, lumbago, pelvic disease, and other things, and most often it has defied our therapeutic efforts, as well as the wisdom of the gynecologist.

Many of these constant backaches—be they mild or severe—acute or chronic—are due simply to a strain or sprain of the sacro-iliac joint.

Just as we twist our foot and get a sprained ankle, so we wrench, from one cause or another, the ligaments holding together the sacrum and ilium, causing a strain or sprain of the sacro-iliac joint.

ANATOMY AND PHYSIOLOGY OF THE SACRO-ILIAC JOINT.

The term sacro-iliac synchondrosis is a misnomer. The more recent investigations of anatomists, obstetricians and orthopedists show that the sacro-iliac joint possesses all the true histological structures of a true joint; that the articulating surfaces of the sacrum and the ilium are covered by cartilage, and this in turn by a thin layer of synovial membrane. So it naturally follows that, being a joint, it must possess a definite amount of motion, although this motion is small in amount, owing to the configuration of the joint surfaces and to the strength and tightness of its ligamentous bindings. This motion has been definitely measured by anatomical observers in the laboratories, and by the obstetrician in his practice. The amount of motion varies under different conditions and is always greater at the time of parturition, when it plays an

important rôle in the mechanism of labor, increasing the superior and inferior straight diameter of the pelvis at different times during labor. The strain on the sacro-iliac joint is tremendous, carrying as it does the weight of the entire torso. When we take into consideration the angle at which the joint is placed and remember the load it has to carry, and that it is a true joint with a definite amount of motion, is it surprising that a strain of the sacro-iliac joint is so very common?

The sacrum may swing in one of two directions, either forward or backward, with the third sacral segment acting as the axis. So we may divide sacro-iliac strain into two classes: Class A, in which the sacrum in its superior border tilts backward. Class B, in which the sacrum in its superior border tilts forward, presenting to us a flat or a hollow back. These two types must be clearly differentiated, for they show an entirely different set of symptoms, are different in their etiology and must necessarily be treated in a totally different manner. Again, either one or both sacro-iliac joints may undergo strain that produces in the one-sided kind a lateral deviation of the spine, while in those cases in which both joints are involved, there is generally no lateral deviation, but simply an increase or diminution in the normal lumbar lordosis.

ETIOLOGY.

Class A, in which the sacrum tilts backward. This is the most important class, so far as the severity of the symptoms is concerned. In this class the etiological factors are numerous, and may be subdivided as follows:

1. *Strains Due to Childbirth*.—As has been stated, the normal amount of motion is increased during the mechanism of labor, so as to increase at different times the superior and inferior pelvic diameter. In many cases of difficult labor, the strain put upon these joints is beyond its normal physiological amount of motion, and the amount of motion therefore becomes pathological, resulting in the disability of the patient for a long period after her delivery. The strain in these cases may be either unilateral or bilateral.

2. *Traumatism (Direct)*.—The strain of the sacro-iliac joint may be due to a direct blow. In my experience, several such cases have been due to cranking an automobile while in gear. The machine, startled from its inactivity, has pushed the patient's sacrum into some neighboring object. Many cases are due to direct violence, such as being struck over the sacrum by heavy timbers; others are due to falls directly upon the sacrum.

3. *Traumatism (Indirect)*.—This constitutes by far the most frequent etiological factor. It is due to muscular strain, caused by the activity of the patient himself while performing some task greater than his muscles will stand, or by some sudden twist, when the muscles hold rigidly and hence throw too much strain upon the ligaments of the sacro-iliac joint. This is well exemplified in stevedores or others who pick up heavy loads while in a stooping position. Athletes, or pseudo-athletes, as golf players, often strain this joint in the swing of the body which follows a drive. Tennis players and ten-

pinists are subject to the same trouble. I can recall the case of a prominent physician who suffered an acute attack of sacro-iliac strain while shoving his boat from the shore with an oar. In fact, occupations that throw an excessive strain upon the quadratus lumborum and erector spinæ muscles, while the muscles of the legs are braced to hold the pelvis firm, will cause a giving away of the ligamentous structure binding the sacrum and the ilium, and thus produce a strain of the sacro-iliac joint.

4. *Static Influence*.—If for any reason one sacro-iliac joint is placed under greater strain than the other, the symptoms will often be referred to that joint. Such is the case when one leg is shorter than the other, as in cases of hip disease, coxa vara, or anterior poliomyelitis of one leg, etc.

5. *Congenital Malformation*.—Occasionally one finds that in the osseous formation of the spine the transverse process of the fifth lumbar vertebræ is fixed into the ilium and sacrum at the articulation; such a condition allows of no motion in the joint. An undue amount of motion necessary for the mechanics of the body is then thrown upon the other sacro-iliac joint, producing the usual symptoms of strain in that joint.

In Class B, when the sacrum is tilted forward, and there is in consequence a hollow back, other etiological factors are the rule.

1. *Static Influence*.—This is particularly the case in girls from 12 to 20 years of age, who have outgrown their muscular strength, and whose muscles lack the tone necessary to keep the body in an erect position.

2. *Neurological diseases*, as anterior poliomyelitis or progressive muscular atrophy, in which again the spinal muscles are involved, and one is no longer able to hold one's self erect.

3. *General visceroptosis*, when all the abdominal organs are markedly misplaced and have drifted from their normal position, even at times into the pelvis. This is particularly noticeable in women, whose continued pregnancies have caused a marked relaxation of the abdominal muscles, which has allowed the visceroptosis to occur. In fact, it might be stated that, as a rule, in Class A the majority of the patients are males, in Class B the women predominate.

4. *Intrapelvic tumors or misplacements*—myomata, sarcoma of the ovaries, or ovarian cysts, indeed, retro- or ante-flexion of the uterus—all tend to a strain of the sacro-iliac joint, with an increase in the lumbar lordosis.

5. *Adiposity*, when the increase of abdominal fat drags on the lumbar spine and the strain is necessarily thrown on the sacro-iliac joints.

These are only a few of the factors causing strain of the joints under consideration.

SYMPTOMATOLOGY.

The symptoms of which patients with sacro-iliac strain suffer vary both in character and degree, according to the severity of the strain, and whether they belong to Type A or B.

In Type A the pain may be mild or severe, so slight as to cause simply an ache across the lumbar and gluteal region on one side, or so severe as to totally incapacitate the patient from

walking, or even lying down. The sciatic nerve passes directly down in front of the sacro-iliac joint, and receives branches from the sacral plexus before it emerges from the sciatic notch. According to the portion of the fiber of the nerve which is pulled upon, whether it be the sciatic, lesser sciatic, or sacral nerves, the pain is referred along these several branches.

Pain in the sacro-iliac joint, therefore, is often felt along the course of the sciatic nerve, even into the calf, and at times into the heel. More often it is referred down the outer aspect of the thigh, and at times it is felt along the crest of the ilium and into the iliac fossa.

Every motion causes pain, and particularly the motions in bending forward or to the side, so that the patient guards them with the greatest care. In the severe cases, the pain and inability to turn is so marked that the patient is not only unable to perform any labor, but is often confined to bed.

In Type B, that of the hollow back, which is most frequently seen in growing girls and neurotic women, the pain is generally referred by the patient to the hollow of the back, and at times as radiating down both thighs. The patients will often describe it as a "tired feeling" rather than an actual pain. Pain of this type is generally worse at menstruation or after unusual exertion or physical prostration. It is also complained of particularly at night, and the patient often sleeps with pillows in the hollow of the back to preserve the unusual lordosis.

DIAGNOSIS.

The diagnosis of sacro-iliac strain is quite simple, but the two types must be differentiated one from the other.

In Type A, where the top of the sacrum is tilted backward, the history is of particular importance, a *history of preceding trauma*, as of a fall, or of being struck by a heavy object in the back, or particularly after some unusual strain on the part of the patient; or, as has been previously stated, the pain has come on after labor.

Pain—referred, acute, or subacute, following and referred along the course of the sciatic, lesser sciatic and sacral nerves.

Pain on direct palpation over the sacro-iliac joint, exerted by pressure from behind. In most cases this pain is elicited on pressure over the upper portion of the joint, but at times it is more pronounced at the lower junction of the sacrum and ilium. Pain may be elicited at times by pressure over both sacro-iliac joints, but generally it is unilateral.

Pain on pressure over the sacro-iliac point in front. Let me call your attention especially to this point, which I have called the sacro-iliac point. It is so often mistaken for McBurney's point that many operations for appendicitis have been erroneously performed on account of its presence. So far as I have been able to gather from the literature, no mention has been made of this point of pain, which is invariably present in all cases of sacro-iliac strain of this type, as well as in inflammatory conditions involving the sacro-iliac joint. It is most constant and is elicited at a fixed point, owing to the structures which cause it, whereas, as we all know, in cases of appendicitis, the pain at McBurney's point may be entirely absent, owing to the wandering proclivities of the appendix.

If the patient is placed on the back, and one makes pressure just to the side and just below the umbilicus, pain will be elicited at that spot on the side in which the sacro-iliac joint is involved.

The next diagnostic sign is the flat back or the obliteration of the lumbar lordosis, due to the tilting of the superior portion of the sacrum backwards, with the third sacral segment as its axis.

Deviation of the Spine.—In bilateral cases there is no deviation of the spine when the patient is in an upright position. But in unilateral cases there is generally deviation of the spine to the side opposite to the sacro-iliac joint involved. This is of marked importance, as it allows us to differentiate the sciaticas which are due to osteoarthritis or infection of the spine, because in this the deviation of the spine is towards the side which is involved.

As the patient bends forward, the deviation of the spine, when present, increases. Bending forward of the spine is more restricted than bending backward, owing to the spasm of the hamstring muscles. Lateral bending of the spine is allowed more freely from the affected joint than toward the affected side.

At times, but rarely, one sees and feels a difference in the amount of prominence of the sacro-iliac articulation on palpation of the sacrum.

Kernig's Sign is Positive.—If one flexes the fully extended leg on the abdomen, the amount of that flexion is naturally limited (Kernig's sign), and pain is referred to the sacro-iliac joint behind. This is due to the contraction and spasm of the hamstring muscles. Kernig's sign is absent in the opposite leg, but at times flexion of the fully extended leg on the abdomen of the good side causes pain referred to the sacro-iliac joint of the bad side.

At times there is an undue mobility which may be made out at the sacro-iliac joint by firmly grasping the ilia in the hands and forcing them together. This, however, is rare, although I have seen it in sacro-iliac strain following the puerperium and in the direct traumatic variety.

There is a total absence of any constitutional features, such as fever, and the blood picture is normal, which would not be the case in certain inflammatory processes of the sacro-iliac joint.

Radiographs.—Whether radiographs will or will not be a help in the diagnosis of the condition, depends upon the type, and whether the strain is bilateral or unilateral. When the condition is bilateral, either in Type A or B, a simple radiograph will not show any deviation of the spine. A stereoscopic radiograph, however, in bilateral cases may show that the articulating surfaces of the sacrum and ilium are out of plumb. In unilateral cases, however, owing to the strain of one joint, the radiograph is a definite adjunct in the diagnosis, for the affected side of the superior edge of the sacrum is tilted not only backward, but also slightly upward, and hence the radiograph will show the spine deviated to the opposite side of the picture. This is due to the list which the top of the sacrum has assumed as a result of the strain.

The diagnostic signs in Type B are different from those in the preceding type. The preceding history of injury is generally absent. It is found mostly in girls between 14 and 20, and in nervous women. The lumbar lordosis, instead of being obliterated, is markedly increased, so that we have the hollow back. The muscular structure is generally below par, both of the spinal and abdominal muscles. Visceroptosis is the rule. The kidneys often are floating and the stomach may lie in the pelvis.

The pain is hardly a pain, but a sense of "always being tired," and tired after slight exertion, or the patient may complain of fatigue when she awakens in the morning. Generally the pain is confined to the small of the back, occasionally going down the thigh a little way.

There is only slight pain to be elicited on direct pressure over the sacro-iliac joint, and rarely can pain be produced by pressing the sacro-iliac joint in the abdomen.

Rarely is there any lateral deviation of the spine, as these cases are almost invariably bilateral, although the pain on one side may be greater than on the other.

Kernig's sign is absent—indeed, flexion of the extended leg generally causes relief rather than pain, as there is no spasm of the hamstring muscles.

Forward bending of the back is not limited, but motion in hyperextension may be restricted.

Pain in most cases of this type is due to the fact that the ligamentous structures of the sacro-iliac joint have to do more than their share of the work in supporting the body. This is due to the weakness of supporting muscles or to direct pull—from pelvic abnormalities or increasing abdominal adiposity.

Differential Diagnosis.—Owing to the drag upon the lumbar and sacral flexors in sacro-iliac strain, the pain is necessarily referred to various portions of the body. It is this fact that so often leads to an erroneous diagnosis.

Tuberculosis of the sacro-iliac joint, in its early stages, offers some difficulty from a differential diagnostic point of view. The pain is situated and referred to such similar localities that other means must be taken to detect it. This can generally be done by keeping in mind the constitutional features of this trouble, with its morning and evening rise of temperature; the blood picture, with its increase in small mononuclear elements; the presence of a cold abscess in the iliac fossa; rectal examination; and the presence of a positive tuberculin reaction, preferably by the subcutaneous method.

Sciatica due to arthritis of the lumbar spine offers some difficulty in differentiation. But this in turn presents an area of tenderness over the lumbar spine on the side of the arthritis. The spine is deviated toward the side of the lumbar arthritis. The X-ray picture shows lipping of the lumbar vertebræ, and possibly deposits of new bone formation. Many cases of sacro-iliac strain have caused these victims to lose their appendices. Pain is often referred down the iliac fossa, and pain at the sacro-iliac point is in many cases mistaken for pain at McBurney's point.

Lumbago is generally a strain of the sacro-iliac joint. We may have a true toxic condition of the muscles of the back,

which we call lumbago, but undoubtedly most cases are due to a strain of the sacro-iliac joint.

Symptoms of this disease closely resemble those of certain pelvic conditions. How many uteri have been suspended and how many vaginæ have been tamponned without relief to the patient? Indeed, the symptoms at times so closely correspond that the gynecologist may not realize his mistake until an exploratory laparotomy is done and no cause for the symptoms found.

TREATMENT.

The treatment which must be instituted to effect a cure in cases of sacro-iliac strain varies according to its severity, and to the type of the case under treatment.

In those cases which we have designated as Type B, when the sacrum is tilted forward, and the pronounced feature is a hollow back, the main principle is to relieve the anterior pulling strain by applying proper support, particularly to relieve the weakened abdominal muscles, and to correct as far as possible the visceroptosis.

In girls and women this can be done by a properly fitting corset, so padded as to support the relaxed stomach and to hold up the floating kidneys. Two extra steels should be incorporated in the corset, on either side of the midline in the back. These steels should not conform accurately to the lumbar lordosis, but tend to diminish it.

Massage and exercises should be given to the spinal and abdominal muscles, so as to increase their power and so relieve the sacro-iliac ligaments of a portion of the strain. It is needless to say that, when the strain is produced by any intra-pelvic condition, it should be remedied by proper gynecological interference.

In cases of this class in men, when the strain is caused by a pendulous abdomen, a proper brace supporting the lower part of the abdomen is of the greatest service.

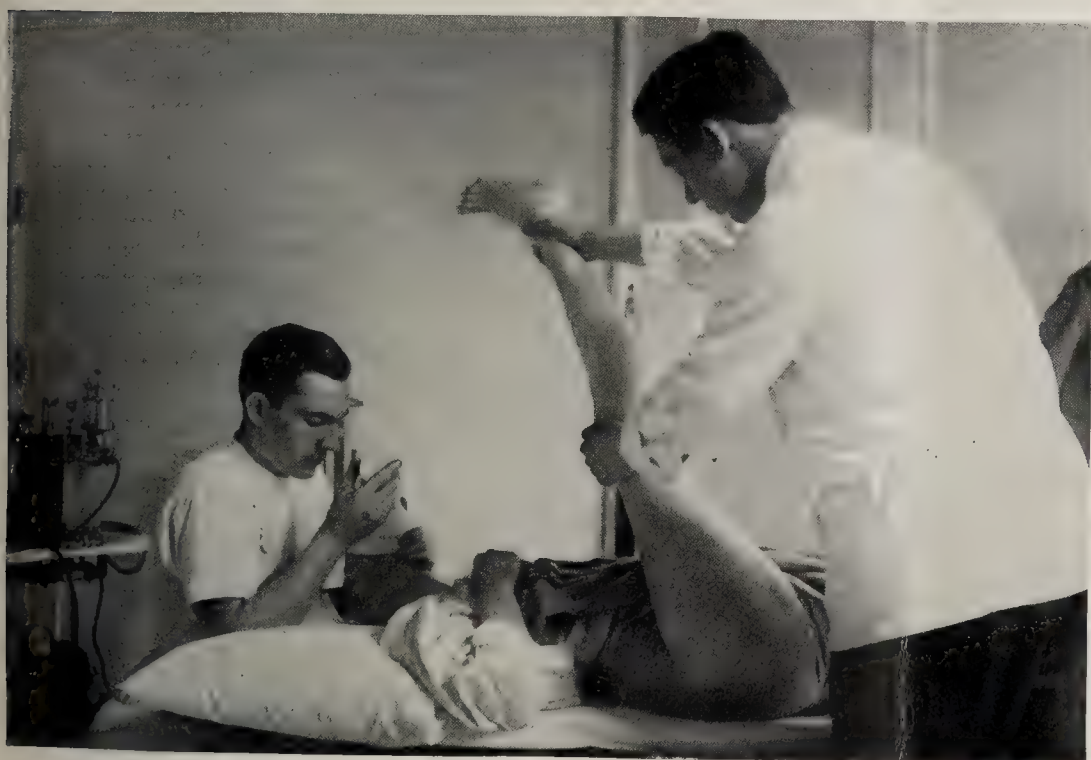
In Class A, when the sacrum is tilted backward and we have the so-called flat back, the treatment is either supporting or manipulatory, according to the severity and chronicity of the particular case.

In acute but mild cases, both in men and women, the greatest possible relief is given by properly strapping the back. An adhesive strap should be placed, going across the buttocks, after the buttocks have been thoroughly compressed—preferably by an assistant—from one trochanter to the other. These straps should be only about 3 inches in their perpendicular width, and should be placed opposite the third sacral segment. Care must be taken that the straps are kept well below the crest of the ilium. They should not extend in front of the trochanters. This will relieve entirely the mild acute forms of the affection.

In cases of a more chronic type, a more permanent brace should be worn for several months. In males this can be done by a surcingle belt, made of buckskin, about $2\frac{1}{2}$ inches in width, which should firmly encircle the pelvis, on a level with the third sacral segment. In cases of males with a large and fatty abdomen, a brace similar to that described in Class B may be used with much benefit.



PLASTER SPICA APPLIED TO PATIENT WHILE STILL UNDER ANÆSTHESIA.



METHOD OF MANIPULATING A CASE OF SACRO-ILIAC STRAIN UNDER ANÆSTHESIA.



DEVIATION OF THE SPINE IN SACRO-ILIAC STRAIN.

In women the corset may be utilized as a support for a webbing belt which is to go around the pelvis; or a sacral pad, made of steel and padded, which gives pressure over the sacrum by its steel prolongations, may be incorporated into the corset.

In those cases of Type A—both in males and females—which have resisted these mild measures, or in severe cases where the pain is very great, the manipulatory treatment is the method par excellence. It is to this method that I wish particularly to call your attention.

We all know of cases of so-called sciatica, painful in the extreme, which have resisted all therapeutic and surgical treatment for months and months, and cases of chronic invalidism, with constant pain in the thigh and an associated limp. Or, we have seen big, strong, healthy men, hardly able to drag themselves into the office or clinic, so great is the pain and disability. These are the cases which respond immediately to manipulation, to the delight of the operator and to the joy of the patient. I have manipulated 100 of these cases, with immediate relief in almost every case, and with a relapse in only three. The procedure is as follows:

The patient is placed on a low, non-movable table, flat on his back, and then anæsthetized. The anæsthetization should be carried to the point of complete relaxation of all muscular tissue, for the force to be exerted at times is great and muscular rigidity carries with it some danger to the patient.

While an assistant holds the pelvis firmly, the operator grasps the calf of the leg and flexes the fully extended limb. The hamstring muscles are found to be in a state of spasm. They are attached to the tuberosity of the ischium at their proximal end, and to the head of the tibia and fibula at their distal extremity. As the fully extended leg is flexed on the thigh, the hamstring muscles pull on the tuberosity of the ischium and the top of the ilium is pulled backward to meet its sacral junction. This procedure of stretching is carried on

until the hamstring muscles are thoroughly relaxed, a condition which is indicated by the fact that the fully extended leg can be flexed to a position far beyond a right angle; indeed, the dorsum of the foot almost touches the shoulder. A definite click is often heard during the manipulation, which some have thought to be due to a replacement of the misplaced sacro-iliac articulation. Of this, however, I am not convinced, for it has seemed to me that the click is to be heard and felt by a slight subluxation of the head of the femur as it pushes against the hamstring while the leg is in extreme flexion. The presence of the click is always synchronous with the release of the hamstring muscles and indicates that the work has been accomplished. If one now looks at the back, one finds that the flat back has been replaced by one with a normal lumbar lordosis. Care should be taken in the manipulation, for it is quite conceivable that, with careless handling, one may obtain a subluxation of the knee joint backward, causing a paralysis, or that one may make a fracture of the head of the femur. The only two complications which have occurred in my series of 100 cases have been in one case, the setting up of a femoral phlebitis, and in the other, owing to my inability to make a proper diagnosis, the production some weeks later of a tuberculous abscess springing from the sacro-iliac joint. After the manipulation has been finished, the patient should be placed on a Goldthwaite frame, and put up in a plaster dressing extending from the nipple line down to the knee on the affected side. This is done to preserve the lumbar lordosis which has been obtained by the procedure.

The patient is allowed to remain in this cast in bed for a period of 10 days, when a small pelvic strap, as indicated for the mild forms, is worn as a preventive measure for the next two months.

I know of no class of cases where the results obtained are so pleasing, both to the patient and his physician.

THE MECHANISM AND CLINICAL SIGNIFICANCE OF ANAPHYLACTIC AND PSEUDO-ANAPHYLACTIC SKIN REACTIONS.*

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Among the earliest authentic records of what are now regarded as anaphylactic reactions is the description of a skin reaction by Jenner in 1798, who observed the sudden appearance of an "efflorescence of a palish red color" about the parts where variolous matter had been applied to the skin of a woman who had had cow-pox 31 years before. Indeed this astute observer taught that the "disposition to sudden cuticular inflammation," following the application of small-pox or cow-pox matter, may be "effected by the small-pox or cow-pox," and that when this sudden local reaction occurred it might be inferred that the person had had one of these diseases and was not now susceptible to either. Strangely enough,

these observations have not attracted the attention they deserve, and even at the present day many physicians fail to recognize or consider the significance of this "immediate or immunity reaction" following cow-pox vaccination among persons who are immune to cow-pox and small-pox, as recently emphasized by Force.

The modern discovery of the local anaphylactic reaction is accredited to Arthus, who discovered in 1903 that the subcutaneous injection of normal serum into sensitized rabbits was followed by a local reaction at the site of injection characterized by inflammatory phenomena, of which edema was a prominent feature. At his time Arthus also showed, that this local reaction was probably an expression of anaphylaxis, inasmuch as these animals would succumb with typical anaphylactic symp-

* Read before The Johns Hopkins Hospital Medical Society, December 4, 1916.

toms following the intravenous injection of the serum. Prior to this time Koch had observed the local reaction following the subcutaneous injection of tuberculin into tuberculous guinea-pigs, but did not suspect the true nature of the phenomenon. In 1907 von Pirquet discovered his tuberculin skin reaction and presented evidence and arguments indicating its anaphylactic nature; since then various skin and mucous membrane reactions have been advocated as convenient and delicate tests for the anaphylactic state to various bacterial and other proteins, in the study of a wide group of pathological conditions.

Whereas the earlier investigations in anaphylaxis were mostly concerned with the clinical manifestations and lesions of the condition, more recently investigators have been mainly interested in the mechanism of the phenomenon and its relation to infection and immunity. For several years my own interests in anaphylaxis have been centered upon skin reactions, and the object of this communication is to present our conceptions of the nature and mechanism of anaphylactic and other skin reactions and their clinical significance as indices of hypersusceptibility and infection, and as indices of resistance to infection or reinfection.

ETIOLOGY OF SKIN REACTIONS.

Tests for skin reactions are conducted by intradermal injection; by application to an abrasion of the skin; by rubbing into the intact skin or, as on mucous membranes, by mere contact, as instillation into the conjunctival cul-de-sac. In the first and second methods trauma, due to the operation itself, is a factor in the production of the resulting inflammation; likewise the intracutaneous injection of practically any protein or non-protein substance will elicit an inflammatory reaction, providing the dose injected is large enough. The causes of various skin reactions may be summarized, therefore somewhat as follows:

1. The *true* or *specific anaphylactic reaction*, due to the interaction in the skin of specific protein antigen and specific antibody.
2. The *pseudo* or *non-specific protein reaction*, due to the interaction in the skin of general protein substances and non-specific proteolysins.
3. The *traumatic reaction* consequent to the operation; or to the irritant qualities of such substances as preformed bacterial toxins and various preservatives, as phenol and tricresol contained in the injected material.

The intradermal test has proven the most delicate means of eliciting a local anaphylactic response, but is also more likely to yield the non-specific and traumatic reactions.

THE MECHANISM OF THE SPECIFIC ANAPHYLACTIC SKIN REACTION.

Although the symptoms and lesions of general anaphylaxis as manifested in man and the lower animals are fairly well understood, the mechanism of the phenomenon cannot be regarded as definitely established; and this is particularly recognized when an attempt is made to correlate the results of an enormous amount of research work in formulating an

explanation of the mechanism of the cutaneous anaphylactic reaction.

Furthermore, an acceptable explanation of the mechanism of cutaneous anaphylaxis must include those truly wonderful urticarial-like reactions which follow within a few minutes the application of a very minute dose of anaphylactogen to an abrasion of the skin, as in those exceptional cases of bronchial asthma and extreme hypersensitiveness to horse or other animal protein, and in hay fever to the protein of various pollens. One of my colleagues who is hypersensitive to the protein of the rabbit, guinea-pig and horse, and who suffers with acute asthma when brought into contact with these animals, yields an immediate typical reaction on the skin when the sera of these animals are applied to abrasions, and indeed to the application of a salt solution extract of lint through which he has inspired for 15 minutes the air of a room in which a few of these animals are kept. Similar and more familiar examples of extreme hypersensitiveness to a protein, and the infinitesimal amounts which may produce an anaphylactic reaction, are to be found in the attacks of hay fever due to the inhalation of air and dust carrying the particular pollen. An acceptable explanation of the mechanism of cutaneous anaphylaxis must, therefore, include these immediate reactions to very small doses of anaphylactogen as well as those reactions which follow some hours, and indeed days, after the intracutaneous or subcutaneous injection of much larger doses of protein.

In the first place, are we justified in assuming that the mechanism of general anaphylaxis and that of cutaneous anaphylaxis are identical? This has been the subject of considerable research over a period of several years in attempts to transfer the specific antibody in animals yielding positive skin reactions to normal animals; by testing animals sensitized at the same time and in the same manner, by the skin test and others, by the intravenous injection of the intoxicating dose of protein; and by first applying the skin test, and after 24 hours injecting the same animals intravenously. The majority of these experiments were conducted with tuberculins and with divergent results and interpretations, but there appears to be sufficient evidence at hand to indicate that a local skin reaction may be an expression of an anaphylactic state to a certain protein, and this is accepted as established in this discussion, although there are not sufficient data at hand to prove that the mechanism of the local or skin anaphylactic reaction is identical with that of the general and fatal reaction following intravenous injection.

At the present time two main theories on the mechanism of anaphylaxis are prominently before us: (1) The humoral or chemical theory, which maintains that the lesions and symptoms of anaphylaxis are due to a poison derived from a protein matrix through the interaction of anaphylactogen and its antibody, or a ferment in the blood and variously designated proteotoxin, anaphylatoxin and serotoxin; and (2) the physical or cellular theory, which denies the formation and activity of this protein poison and maintains that the anaphylactogen unites with its antibody in the cell, and that this union results in a disturbance causing shock of the cell.

The two schools agree at least in two points, namely, that an antibody is concerned in the phenomenon of anaphylaxis, and that the anaphylactogen is always of a protein nature. Neither has very clear conceptions of the nature and mechanism of action of the antibody; whereas the adherents of the cellular theory maintain that the foreign protein constitutes the anaphylactogen, the adherents of the chemical theory, are divided in their opinions regarding the protein matrix, some regarding the matrix as the foreign protein and others as the protein of the patient's own serum.

The older conception of the antibody, that held by Friedberger, and widely accepted to-day, is to the effect that it belongs to Ehrlich's group of amboceptors or lytic antibodies of the third order. As is well known, an antibody of this nature, according to Ehrlich's theory, is produced through the influence of the antigen (bacteria, serum, egg albumen, pollens, etc.) upon the body cells, and is specific for the antigen in so far that it will unite only with its antigen and prepare the latter for the disrupting, digesting or lytic action of a ferment-like substance normally present in the blood and called complement. In this manner the antibody producing the protein poison of anaphylaxis has the same structure and acts in the same manner as other well-known antibodies of this order, namely, the hemolysins and bacteriolysins.

According to this view we must concede that complement plays a rôle, indeed a most important one, in the production of anaphylaxis. While complement has properties suggestive of a proteolytic ferment, we know little or nothing of its true nature beyond that it is regarded as essential for the cleavage of the antigenic molecule. Sleeswijk,¹ Friedberger and Hartoch,² Loeffler³ and others have shown that complement is diminished during anaphylactic shock; likewise Friedberger,⁴ making use of the observations of Nolf⁵ and Hektoen⁶ to the effect that complement is not bound by antigen and antibody in the presence of hypertonic salt solution, devised experiments which appeared definitely to establish the rôle of complement in the production of a protein poison and in the mechanism of anaphylaxis.

Test-tube experiments, and particularly efforts to explain anaphylaxis on the basis of the Abderhalden theory and technique, seriously question the rôle of complement in the mechanism of anaphylaxis. Williams and Pearce,⁷ Lange,⁸ Jobling, Eggstein and Petersen,⁹ and Kolmer and Williams,¹⁰ found that digestion occurred with activated serum, but to a lesser degree than results with active serum. On the other hand, Stephan,¹¹ Hauptmann,¹² Bettencourt and Menèzes¹³ and Steisung¹⁴ believe that a complement plays a very important rôle in Abderhalden's test. Abderhalden, himself, while believing that the serum complement plays some part in the mechanism of his reaction, but in a different manner than in hemolysis or other cytolytic reactions, offers no adequate explanation of its relation to these processes.

It would appear, therefore, that if we attempt to explain anaphylactic reactions, either general or local, by an application of the well-known theory of antigen-amboceptor-complement production of the anaphylactic poison on the basis of

experiments *in vitro*, we must prepare ourselves to believe that the actual lytic or digestive body in the serum (call it complement or true enzyme) exists in both a thermolabile and thermostabile condition. Whereas hemolysis, bacteriolysis and other cytolytic reactions will occur only in the presence of fresh complement serum, the protein poison of anaphylaxis may be produced apparently by an active or an inactivated serum; otherwise it would appear that an explanation of the mechanism concerned in the production of anaphylatoxin must be withdrawn from the field of amboceptor-antigen-complement activity, as understood at present.

Vaughan has always called the antibody in the serum concerned in the mechanism of anaphylaxis a "ferment"; likewise Abderhalden and Jobling and Petersen have used this term. As far as I know, these observers have not clearly defined the meaning of the term "ferment"; nor have they established its relation or lack of relation to the amboceptors of Ehrlich or sensitizers of Bordet; apparently they regard the "ferment" as a proteolytic enzyme or protease. This conception of the enzyme nature of the "ferment" would correspond somewhat with the non-specific alexin of Bordet, or Ehrlich's complement, and fail to harmonize with the specific nature of anaphylaxis. Otherwise it is necessary to believe that the entrance of a foreign protein calls forth the production of a specific proteolytic enzyme or ferment capable in itself of attacking and disrupting a protein matrix, and, as stated above, to place the mechanism of anaphylaxis out of the realm of amboceptors and complements according to the theories of Ehrlich and Bordet.

The trend of more recent work in the mechanism of anaphylaxis by Jobling and Petersen¹⁵ is in this direction. These investigators have produced a protein poison *in vitro* by chemical methods in such manner as apparently to rule out the influence of the thermolabile and easily destroyed complement or alexin. According to their views, serum complement and normal proteolytic ferments are not identical and, whereas the former may be inactivated by heating at 56° C. for half an hour, the latter are more resistant, the increased digestive power observed following the addition of serum complement to inactivated pregnancy serum being ascribed to the amounts of non-specific protease thereby added.

It is clear, therefore, that in the humoral or chemical theory of anaphylaxis the true nature of the antibody is unknown and in dispute; Friedberger¹⁶ was among the first to maintain that the antibody is identical with precipitin. More recently, Lake, Osborne and Wells,¹⁷ Doerr and particularly Weil,¹⁸ the last being an ardent advocate of the cellular theory of anaphylaxis, are inclined to the same view without, however, offering a clear explanation of its action *in vivo* in the mechanism of anaphylaxis. While the rôle of precipitins themselves appears to have been excluded as directly participating in the production of anaphylactic shock, recent experiments by Zinsser¹⁹ and others would tend to show that a precipitin possesses the nature of a protein sensitizer or antibody that sensitizes or prepares the protein antigen for lysis or destruction.

As previously stated, the chemical and cellular theories of anaphylaxis agree that the anaphylactogen is always a protein. In the cellular theory the anaphylactogen is regarded as specific, and this is in accord with accepted facts regarding the high specificity of the anaphylactic reaction; in the chemical theory, however, there is no agreement, some maintaining that the anaphylatoxin is derived from the foreign poison or anaphylactogen, and others that it is derived from the protein of the patient's own serum.

The view first held in the chemical theory is that in the anaphylactic reaction the antibody acts upon its protein antigen in a specific manner and produces in the reaction the protein poison or anaphylatoxin responsible for the lesions and symptoms of the anaphylactic reaction. For example, during an infection with the spirocheta pallida, an antibody is produced which, acting upon an emulsion of dead spirochetes (luetin) injected into the skin, splits the protein of these parasites in a specific manner with the production of a poison responsible for the local reaction of erythema and infiltration.

An anaphylactic reaction of this kind, a cellular or formed antigen being employed, is regarded as being divided into two phases. As compact structures, cells cannot enter into direct chemical relations with the fixed tissue cells until they have been resolved or disintegrated into simpler constituents by ferments or antibodies in the body fluids. This is followed by the second phase, or the interaction of the anaphylactic antibody and the dissolved antigen. Anaphylactic reactions with such formed elements as erythrocytes and bacteria may occur; usually it is more difficult to sensitize the body cells with these antigens than when dissolved proteins, as in blood serum, are employed.

The experiments of Keysser and Wassermann,²⁰ Bordet,²¹ Jobling and Petersen,²² Plaut,²³ Peiper,²⁴ Friedemann and Schönfeld,²⁵ Bronfenbrenner,²⁶ and others, tend to show that the mechanism is not quite so simple and direct, and that a protein poison may be produced in the absence of the specific antigen. They have demonstrated by experiments *in vitro* that such inert substances as kaolin, barium sulphate, agar or indifferent bacteria or precipitates may replace the antigen in the production of a protein poison. Since the presence of protein substances could be excluded, as with such inorganic substances as kaolin and barium sulphate, the conclusion was naturally drawn that the matrix of the poison was not the antigen or substrate, but the constituents of the serum itself. Jobling and Petersen advanced the theory that the proteolytic ferment was held in check by antiferments (largely the unsaturated fatty acids in serum), and that these substances, as kaolin or barium sulphate, absorb the antiferments and thereby release the proteolytic ferments which proceed to digest the protein of the serum. For this reason these investigators have applied the name "serotoxin" to the protein poison as indicating its source.

Applying these observations and views to the subject under discussion, it would appear necessary to infer that the antigen is non-specific and acts as it were in a purely mechanical manner; this does not at all agree with the great mass of data show-

ing the highly specific nature of anaphylaxis. In tertiary syphilis, for example, the reaction in the skin following an injection of an emulsion of dead spirochetes (luetin) would be due, according to this mechanism, not to a digestion of the protein of the spirochetes with the production of a protein poison, but the luetin would act simply as a local absorbent of the antiferment, releasing thereby proteolytic ferments which proceed to digest the patient's own serum or cellular protein *in loco* with the production of a poison responsible for the reaction; and if this were true, the reaction lacks specificity.

Bronfenbrenner²⁷ explains the specific production of anaphylatoxin by non-specific ferments or antibodies as follows:

Specific antibodies are produced, and the combining of these with the antigen causes a falling out or inactivation of the antiferments of the serum by a change in colloidal conditions resulting in the release of normal or non-specific proteolytic ferments which disrupt or digest the protein of the serum. In other words specific antibodies are produced, but instead of these digesting the protein of the antigen or of the serum directly, they act by uniting with the antigen, and this union results in the removal of anti-enzyme, thereby releasing or rendering active the normal and non-specific enzymes of the serum which produce a protein poison or anaphylatoxin, by digesting the protein of the serum.

Whether or not the results of a study of the mechanism of Abderhalden's reaction—which in the final analysis is nothing more than a popularized method of studying protein digestion in a manner pregnant with opportunities for error—can be applied to unfolding the mechanism of anaphylaxis is uncertain; but it is certain that an explanation of the mechanism of either the local skin or general anaphylactic reaction must satisfactorily explain the high and uniform specificity of these reactions before it is acceptable.

The above-mentioned experiments, which have been largely conducted *in vitro*, are not without definite value and, as I shall point out later, have a greater bearing upon the mechanism of the pseudo than upon the true anaphylactic reaction and the phenomena of local inflammation in general.

Up to this point our discussion has been confined to present-day conceptions of the nature of the protein matrix, the mechanism of action of the antibody or ferment according to the clinical theory, and the effects of the protein poison on body cells in anaphylactic phenomena.

No discussion is complete, however, without particular reference to that peculiar change on the part of the cells, probably involving the colloidal chemistry of the cells themselves, which exerts so important a rôle in anaphylaxis, and particularly in the local reaction. This altered reactivity of the cells, or their unusual and exaggerated susceptibility to the effects of the products of digestion of foreign proteins, was early emphasized by von Pirquet, by Rosenau and Anderson, and by other pioneers in this field; and on account of the importance of this phase the former proposed the term "allergy," meaning "altered reactivity," as describing the phenomena more concisely than Richet's term "anaphylaxis," meaning "without protection." The term "allergy" is in our opinion more

appropriate, as it emphasizes the important hypersensitiveness or altered reactivity of the cells, regardless of any theories we may entertain as to the manner in which this change is brought about or manifested.

Definite information on the nature of this peculiar cellular change is lacking. When one bears in mind the intense local, focal and general reaction in tuberculosis that may follow the injection of a minute amount of tuberculin, or the minute amount of protein that suffices to induce the anaphylactic reaction in the classical experiment with horse-serum and guinea-pigs, conditions in which the amount of protein poison produced must be very slight indeed for physical reasons alone, the supposition is forced upon one that some change rendering the cells highly susceptible to the anaphylactic poison is of fundamental importance in anaphylactic reactions.

Investigators have attempted to explain this peculiar hyperactivity of the body cells on the basis that the reaction is a cellular one, that is, that the antibody is within the cell and that the antigen-antibody reaction occurs in this position rather than in the blood-stream by means of free or circulating antibody and antigen. According to the "cellular theory," if the serum of an immunized animal containing the anaphylactic antibody is injected into a normal animal (passive anaphylaxis) and is followed by an injection of the antigen, an anaphylactic reaction cannot occur before the elapse of sufficient time for the antibody to become anchored to cells. The "humoral theory," on the other hand, assumes that the antigen meets the antibody in the blood-stream and explains the time required between the injection of immune serum and antigen in passive anaphylaxis as due to a failure of rapid union between antigen and antibody, unless quantitative relations between the two are accidentally correct.

The early theory of Friedberger,¹⁸ explaining anaphylaxis on the basis of "sessile receptors"; the experiments of Friedberger and Girgolaft,²⁸ who passively sensitized normal animals by transplanting the thoroughly washed organs of a sensitized animal; the transfusion experiments of Pearce and Eisenbrey,²⁹ who transferred the blood of a sensitized animal to a normal animal, and the blood of a normal animal to a sensitized one, finding that the latter, but not the former, reacted when the antigen was injected as soon as the transfusions were completed; the work of Coca,³⁰ who found that sensitized guinea-pigs would still react after being thoroughly bled and perfused with salt solution; the investigations of Schultz,³¹ Dale,³² and particularly of Weil,³³ showing that the excised and washed muscles of sensitized animals would react *in vitro* in a bath of Ringer's solution when the antigen was added, support most strongly the cellular theory of anaphylaxis as emphasized also in the work and recent communications of Doerr.³⁴

In the opinion of Weil, Doerr, Bayliss, Coca and others, the "cellular" theory is the only tenable one to-day. According to this theory of anaphylaxis, the antibody is in or on the body cells; upon union with the antigen, the cells undergo a physical shock which has been likened to an electrical shock, and this constitutes the basis of the anaphylactic reaction without the formation of any intermediate or chemical poison.

As emphasized by Weil,³³ there is no direct evidence of the production of a chemical poison or anaphylatoxin during or after an anaphylactic reaction in the living animal. This poison has not been satisfactorily demonstrated in the blood and in animals recovering from a general anaphylactic reaction, the phenomena being more suggestive of a transitory "shock" than of an intoxication with a chemical poison.

On the other hand, the mass of experimental evidence indicating that the anaphylactic reaction is not purely cellular, but at least in part an intravascular reaction, is too strong to be discarded. As pointed out by Zinsser and Young,³⁵ the necessary time usually required in passive anaphylaxis between the injection of immune serum and antigen may be due to slow union between antigen and antibody in the blood-stream, on the basis that the anaphylactic reaction involves the interaction of colloids and that a protective colloid is responsible for the slow union of antigen and antibody, unless its influence is obviated by exact quantitative proportions between antigen and antibody, which under experimental conditions may be secured in a more or less accidental manner.

As antibodies are produced by the body cells, it is reasonable to believe that they are present in the protoplasm of the cells, and even after thorough washing of the tissues are capable of union with their antigen. It is entirely likely that these attached or sessile antibodies are chiefly concerned in the phenomena of anaphylaxis, but I cannot subscribe entirely to the cellular theory, because of the mass of experimental data bearing on the production of the protein poison, particularly *in vitro*, by the free antibodies in an immune serum. The reactions *in vivo* of hemolysis and bacteriolysis, which are lytic processes, apparently similar to those concerned in anaphylactic reactions, are probably intravascular processes; it is also likely that in anaphylaxis to formed antigens the first phase of the reaction, that is, the disruption of the antigenic cell, is intravascular, showing that lytic reactions entirely analogous to our conception of the mechanism of the production of the protein poison in anaphylactic reactions may occur in the blood serum. For these reasons alone I cannot exclude the free antibodies in the blood from playing some rôle in the phenomena of anaphylaxis.

The extreme sensitiveness of the body cells in anaphylaxis to the protein suggests to me that the cells acquire the property of union with the protein poison to an extreme degree, as if they were furnished, as a result of the initial dose of foreign protein, with an increased number of specific and sessile receptors for the protein poison. In other words, while the protein poison may be produced in the cells by sessile receptors, or in the blood-stream by free receptors, anaphylaxis itself, that is, the hypersensitiveness of the cells is due to the increased binding power of the cells for the protein poison. In our opinion this in part explains true allergy, that is, the effects of local or general sensitization (production in the protoplasm of the cells of increased receptors for the protein poison) and the immediate well-marked or even violent effects following the production of what must be very minute amounts of protein poison, as in the cutaneous tuberculin reaction, or in the

classical horse-serum reaction in guinea-pigs following the intravenous injection of the intoxicating or second dose of protein in very minute or infinitesimal dosage.

Personally I should be more prepared to understand and accept the cellular theory in the strictest sense in the mechanism of anaphylaxis, were my studies confined entirely to general anaphylactic shock; in the local reaction, however, the slowly spreading character of the lesion, the erythema, edema and eosinophilic infiltration strongly suggest that a diffusible irritant has been produced similar, in some respects at least, to that which can be produced *in vitro*.

As far as I am aware, the skin or local anaphylactic reaction has not been explained on the basis of the cellular theory alone in its strictest sense. These reactions have many of the features of an inflammatory reaction, of which vascular changes (hyperemia) and edema are prominent features. Intracutaneous reactions are likely to persist for several days; likewise the cutaneous tuberculin reaction, although the cutaneous reaction to pollen and serum may reach its height within half an hour and disappear within a few hours. May these inflammatory-like changes be ascribed to a temporary and physical shock of the endothelium of vessels in the skin, followed by stasis and exudation, and of the connective-tissue cells at the site of injection? As previously stated, I believe that the cells play the major rôle in anaphylaxis, in that the formation of a diffusible protein poison occurs largely in or on the cells by reason of the fact that the antibodies are largely situated in the cells and that the cells bear the brunt of the change and undergo shock by reason of the poison being produced in them, but I also believe that a poison is produced which may escape detection by high dilution in the body fluids in the general reaction, but which appears in the local reaction as a diffusible irritant, producing the phenomena of acute congestion, edema and leucocytic infiltration (particularly of eosinophiles).

It is my opinion that the source of the protein poison in true anaphylaxis is always that which has been injected and for which specific antibodies are present mainly in the cells.

I regard cutaneous anaphylaxis as due to an interaction between true or specific antigen and its specific antibody with the production of a diffusible irritant capable of exciting inflammation; that this union of antigen and antibody occurs principally within the cells, and that the cells suffer largely by reason of this interaction and formation of irritant within them.

An adequate explanation of those apparently anaphylactic reactions to drugs has not been made. It is generally held that the drug alters a body protein with the formation of a new protein compound capable of sensitizing and producing anaphylaxis. Recently my colleague, Dr. Fred Boerner, who is hypersensitive to quinine and suffers considerably with cutaneous manifestations, if even minute doses are swallowed, has shown me a marked reaction of edema and erythema in his skin following in a few minutes the application of powdered quinine sulphate or a solution of the bisulphate to an abrasion. He has shown that this reaction is apparently specific, inasmuch as it does not occur among persons not hypersensitive to quinine,

and a similar reaction occurred in the skin of a second person known to be hypersensitive. The occurrence of these reactions within a few minutes after the application of quinine renders the theory of the formation and activity of a new protein compound doubtful.

MECHANISM OF NON-SPECIFIC PROTEIN AND TRAUMATIC SKIN REACTIONS.

It appears well established that the blood-serum, leucocytes and the fixed cells of various tissues of the body contain proteolytic ferments capable of digesting various protein substances *in vitro*. The digestive activity of these ferments can be studied and determined only by very delicate methods, and are apparently non-specific in character.³⁷ *In vitro* they apparently are capable of producing toxic substances which may be regarded as protein derivatives. These proteolytic ferments may be responsible for local inflammatory phenomena, and in an attempt to correlate these results with the mechanism of the non-specific and purely inflammatory reaction which may be the sole reaction in the skin and lead to misinterpretation and error, or occur coincidentally with the true anaphylactic reaction, the following explanations have been offered:

1. An irritant is produced through the interaction of general proteolytic ferments and various proteins injected, as those contained in broth, agar or ascitic fluid. This irritant or chemical poison is responsible for the lesion.
2. Trauma caused by the needle, or trauma plus injury to the cells, due to the presence of a preservative as phenol or tricresol, or a preformed toxin (as the diphtheria toxin used in the Schick test), or a bacterial protein of an irritant nature, may destroy a sufficient number of cells to release their proteolytic ferments which proceed with a process of digestion; or the injection mass and dead cells mechanically absorb the antiferment and thereby activate the ferments which produce from the injected protein, or that of the dead cells and patient's own serum, sufficient proteotoxin to bring about an inflammatory reaction.

The injection into the skin of a foreign protein (the anaphylactogen) as that protein present in sterile bouillon or, for example, the protein of bouillon, agar and spirochetes as present in luetin, increases the production of protein poison by more active release of proteolytic ferments through removal of the antiferments by absorption or in some other way, followed by digestion of the injected protein and the protein of the patient's devitalized cells and serum.

This protein poison or proteotoxin is an irritant and excites inflammation of varying degrees of severity. In this manner we have a ready explanation for those pseudo-reactions following the intracutaneous injection of sterile broth, as found by Kolmer and Moshage,³⁸ of extracts of placental cells by Engelhorn and Wintz,³⁹ Falls and Bartlett,⁴⁰ Kolmer and Williams,⁴¹ of agar and emulsions of normal and pathologic skin by Stokes,^{42 43} of heated diphtheria toxin-broth by Zingher,⁴⁴ and various other protein substances by various investigators.

It is highly probable that the quantity of proteolytic fer-

ments in the cells and serum of different persons vary, and that the quantity of ferments in the cells of the skin of the same person varies in different areas of the body; and in this manner could be explained the varying degrees of non-specific or purely inflammatory reactions in the same person in different parts of the body, or among different persons, after the injection of the same protein in the same dosage. Dr. Moshage and I have found that the skins of persons convalescent from scarlet fever and measles are especially prone to yield these non-specific reactions.

Any protein substance, if injected into the skin in sufficiently large amount, will elicit a non-specific or inflammatory reaction. For this reason the material used in conducting skin tests for the specific anaphylactic reaction should be carefully prepared and administered in such amount as will not elicit a non-specific reaction among a large number of controls; and the injection of a control fluid is always advisable. Cutaneous tests are much less likely than intracutaneous tests to yield non-specific reactions of sufficient degree to prove disturbing; they are less delicate tests for the anaphylactic state, but also less open to error.

THE INFLUENCE OF DRUGS UPON SKIN REACTIONS.

Recently Sherrick⁴⁹ has reported that normal persons under the influence of iodides would yield positive reactions to the intracutaneous injection of luetin. Broadwell, Matsunami and I⁵⁰ were able to confirm these observations, in that a normal person who had reacted negatively to luetin in the preliminary test would frequently react to a well-marked degree when the test was applied after the administration of potassium iodide. We also observed similar results among rabbits and guinea-pigs.

During the past year these studies have been continued with the cooperation of Dr. Immerman, Dr. Matsunami and Dr. Montgomery,⁵¹ various iodides, bromides, chlorides and anesthetics and two intracutaneous tests, namely, the luetin test and one with an emulsion of *B. prodigiosus* being employed. Both tests were made beforehand upon Wassermann-negative persons, and repeated after the administration of from 90 to 170 gr. of the drugs, or after operation under ether or nitrous oxide. Iodides and bromides were found to exert a considerable influence, whereas the influence of chlorides was much less in evidence, and ether and nitrous oxide were without demonstrable effect.

According to Jobling and Petersen, the antiferment of the serum is of the nature of unsaturated fatty acids, and these may be removed by the halogens and the ferments thereby released or rendered active. The influence of these drugs upon skin tests may, therefore, be explained upon this basis. We are of the opinion that they do not influence the mechanism of true anaphylactic reaction, but only the non-specific or simple inflammatory portion of a skin reaction by facilitating the release of non-specific ferments. This opinion is based upon the observation that the influence of these drugs upon skin reactions has been observed in persons who were not anaphylactic to the protein; that much less influence was observed

upon true anaphylactic reactions to the cutaneous application of tuberculin, and that the greater the amount of bacterial protein or culture medium constituents injected the severer the reaction.

Since the non-specific element may always play a part in skin reactions following intradermal injections, it is well for physicians to bear in mind that these drugs may so favor the non-specific reaction as to present evidences of a violent reaction which may be interpreted as anaphylactic.

THE CLINICAL SIGNIFICANCE OF ANAPHYLACTIC SKIN REACTIONS.

1. *As Indices of Hypersusceptibility and Infection.*—The clinical significance of a true anaphylactic skin reaction to a certain protein, aside from establishing the fact that a person is hypersensitive to that protein, depends upon what harm may be done with the enteral or parenteral introduction of the protein. It is not my purpose to review in detail the many clinical conditions which appear to be due to a state of anaphylaxis; this phase of the subject has been recently covered in a thorough and excellent manner by Longcope.⁵² Here it may be recalled that examples of apparently true spontaneous hypersensitiveness to various foreign proteins are not uncommon and, indeed, the trend of recent investigations is always widening this field and establishing hypersensitiveness as a probable basis for many diseases with symptoms referable to the respiratory tract, gastro-intestinal tract, and the skin. In the minds of not a few physicians the term "anaphylaxis" means a brief and stormy general reaction following the administration of diphtheritic antitoxic horse-serum, a reaction occupying, as it were, a distinct and isolated place in the field of immunity, whereas this is but one manifestation of a process which bids fair to become established as the basis of many and diverse clinical conditions, as, for example, hay fever, ivy poisoning and similar toxic dermatoses, bronchial asthma, serum sickness and that wide field of various food idiosyncrasies due to the ingestion of eggs, milk and various meats as studied by Schloss,⁵³ Lesné and Richet,⁵⁴ Talbot,⁵⁵ Smith,⁵⁶ Strickler,⁵⁷ Blackfan,⁵⁸ and others. I have been particularly interested in the investigations conducted in my laboratory by Strickler, which show the very important relation of hypersensitiveness to various vegetable and animal proteins to eczema and other skin diseases.

Further researches will show us what harm may be done by the anaphylactic poison; at present we know that grave symptoms and even death may result from the parenteral injection of a serum to which a person is highly susceptible; Longcope and his co-workers have shown that the poison may produce slow but definite degenerative lesions in the kidneys; the ingestion of eggs or other food by a person hypersusceptible to their protein is known to produce symptoms and skin manifestations which disappear or are ameliorated upon the permanent withdrawal from the diet of such foods. In other words, evidence is accumulating to show that hypersensitiveness plays an active rôle in the etiology of many diseases, and in the detection of

these skin reactions are proving of great value and indeed may prove the only means of specific diagnosis.

As is well known, anaphylactic skin reactions may be elicited in various bacterial and protozoan diseases with anaphylactogens prepared from the protein of the respective microparasites, particularly in tuberculosis, glanders, typhoid fever and syphilis. Well-marked and specific reactions have also been found by Amberg⁵⁰ and by Kolmer and Strickler in ring-worm and favus, and isolated reports show that they may be elicited in various other diseases with proper preparations.

In these conditions, however, the skin reactions are not always elicited, and especially during the early and acute stages. An interval of time is required for the purpose of sensitization, and during the acute stages antigen and antibody may both be present in the cells and body fluids, as shown by Weil⁵¹ and Denzer,⁵² with continual interaction expressed in the symptom-complex of the infection, and thereby giving no response when the protein is applied or injected into the skin. Furthermore, the chemical nature of the protein of our anaphylactogen may have been altered in the course of preparation to a sufficient extent to fail to elicit an anaphylactic reaction. These and other factors not understood diminish the practical value of a skin test. At present, however, it may be stated that they possess a diagnostic value which is particularly high in chronic infections, and that no other satisfactory clinical or laboratory test for the state of anaphylaxis to a particular protein and for the anaphylactic antibody has been discovered, except that by which the protein is actually brought into relation with the body cells, as in the parenteral introduction of the protein. Of great interest in this connection is the relation of the intensity of the anaphylactic skin reaction to the extent of the infection. Krause⁵³ has recently studied in a thorough and excellent manner the tuberculin skin-reaction in relation to experimental tuberculosis, finding that cutaneous hypersensitiveness to tuberculo-protein is inaugurated by the establishment of infection and the development of the initial focus; that the skin-reaction increases with progressive disease; is diminished with healing and increased by reinfection.

2. *As Indices of Immunity.*—Of further importance is the question of the clinical significance of a local anaphylactic reaction as an index of immunity, that is, resistance to an infection or reinfection. Is the anaphylactic antibody capable of attacking and destroying the antigenic protein in a living state? Are protective and curative antibodies produced by the defensive mechanism of the body, while the cells are being sensitized and the anaphylactic antibody is being produced? In other words, is hypersensitiveness to be regarded as an index of resistance?

In 1798 Jenner wrote: "It is remarkable that variolous matter, when the system is disposed to reject it, should excite inflammation on the part to which it is applied more speedily than when it produces the small-pox. Indeed, it becomes almost a criterion by which we can determine whether the infection will be received or not." In other words, as previously mentioned, this astute observer noted that a person who presented within a few days at the site of vaccination an

"efflorescence of palish color" was probably immune to small-pox. Force⁵⁴ has recently drawn attention to this "immediate" reaction to inoculation with cow-pox virus as an evidence of resistance or immunity to cow-pox and small-pox, and my own experience supports his conclusions. Here, indeed, we have evidence at hand indicating that an anaphylactic state is an index of the coincident presence of antibodies and resistance.

Investigations bearing upon the relation of anaphylaxis to immunity in other infections have not generally yielded these results. Rosenau and Anderson⁵⁵ sensitized pigs with extracts of *B. typhosus* and *B. coli*, and found that animals so treated were immune to amounts of the respective microorganisms fatal to normal pigs; Romer⁵⁶ and Sata,⁵⁷ in experiments among cattle with *B. tuberculosis*, reached the conclusion that a state of hypersensitiveness meant a certain degree of resistance, while Krause⁵⁸ and Austrian⁵⁹ have expressed the opinion based upon experiments, that sensitization of non-tuberculous animals with tubercle protein does not raise their resistance to experimental tuberculosis infection and indeed may lower it.

More recently Gay and Force⁶⁰ have greatly renewed interest in this subject by advocating the skin test as a means of determining defensive activity following typhoid fever or active immunization by means of vaccines. Their first work was conducted with a "typhoidin" prepared in the same manner as Koch's old tuberculin by cutaneous inoculation. Later, Gay and Claypole⁶¹ prepared typhoidin by precipitating the solution with alcohol, washing the precipitate with alcohol and ether, drying in a vacuum and suspending the resulting powder in phenolized normal salt solution, which was injected intracutaneously and applied cutaneously, a control powder being prepared from broth and used in the same manner. With this skin test, Gay and his associates have studied the relative value of various vaccines and regard the anaphylactic reaction as indicative of a state of immunity. Nichols⁶² has questioned the value of the anaphylactic skin test as an index of immunity and regards the typhoidin reaction as indicating nothing more than sensitization to typhoid protein, which is apparently less lasting and less specific than the true immunity to this infection. He bases this opinion on the fact that in his experience the typhoidin skin test gave fewer positive reactions (75 per cent) than were generally expected, since about 90 per cent of persons who have had typhoid fever are immune for many years, or even for the balance of life. Furthermore, according to Nichols, experience has shown that protection following typhoid fever is of longer duration than is indicated by the typhoidin test, and although a large percentage of persons who have had typhoid fever or have been immunized with typhoid vaccine react to paratyphoidin, recent experiences and statistics, particularly in Europe, have indicated that these persons are not immune to paratyphoid fever.

My own experiments in this field have been largely tests *in vitro* for various antibodies as agglutinins, bacteriolysins and complement-fixing substances in the fresh sterile blood sera of persons hypersensitive to various proteins, in order to determine whether or not the state of hypersensitiveness to a particular bacterial protein was accompanied by demonstrable

amounts of these antibodies. I am well aware of the shortcomings of such tests and that the weight of opinion minimizes their value as an index of actual immunity. As previously mentioned, Friedberger¹⁶ was among the first to maintain the identity of precipitin and the anaphylactic antibody; Doerr and Russ¹⁷ independently reached the same conclusion, and more recently Lake, Osborne and Wells¹⁷ and Weil¹⁸ have brought forward a considerable amount of evidence in support of the view that precipitins are frequently present in the serum of the sensitized animal.

The experiments conducted by Mr. Berge and the author¹³ with reference to the typhoidin skin reaction showed that while the bactericidal power of human serum over *B. typhosus* is increased in a proportion of persons following typhoid fever or active immunization with a vaccine, there is no direct relation between the typhoidin skin reaction and the results of bactericidal tests *in vitro*. Likewise, no definite relation was observed between the presence of agglutinins and complement-fixing antibodies and the skin reactions.

A similar study in syphilis by Broadwell and the author¹³ has shown that in human syphilis spirocheticidal antibodies for culture pallida are practically absent from the sera of those persons who do and who do not react to the intracutaneous injection of luetin. Likewise, no constant relationship was found between the occurrence of cutaneous hypersensitiveness to luetin and the presence of agglutinins for culture pallida and of a complement-fixing antibody with an antigen of luetin.

Similar studies in diphtheria by the author¹⁴ likewise showed an absence of any relationship between cutaneous hypersensitiveness to a polyvalent and detoxized emulsion of diphtheria bacilli or diphtherin,¹⁵ and the presence of such antibodies as antitoxin, agglutinin, bacteriolysin and complement-fixing substances for diphtheria bacilli.

Additional studies by Harkins, Matsunami and the author,¹⁶ along similar lines in canine distemper, have shown that the sera of dogs reacting positively to the intracutaneous injection of a polyvalent emulsion of *B. bronchisepticus*¹⁷ do not show the presence of agglutinins, bacteriolysins and complement-fixing antibodies for this bacillus in any constant relationship to the skin reactions.

In a strict sense the question whether or not an anaphylactic skin reaction may be taken as an index of defensive activity can only be answered on the basis of actual protective experiments. Time alone will tell whether or not the person presenting a positive reaction to typhoidin is actual immune to typhoid fever as claimed by Gay and his associates. Experiments among rabbits with cultures of *Spirocheta pallida* by Noguchi,¹⁸ consisting in the immunization of the animals until they reacted to the intracutaneous injection of luetin, followed by an actual test of their immunity to living virulent spirochetes by inoculating the testicle, have given Dr. Noguchi the impression that the immunization reduced susceptibility in some rabbits, whereas it had no effect whatsoever in others, and indeed seemed to render some more susceptible. Furthermore, it is highly probable that the syphilitic is open to reinfection with *Spirocheta pallida*; certainly our experiments

failed to show the presence of appreciable amounts of spirocheticidal antibodies in the sera of tertiary syphilitics reacting positively or negatively to the intracutaneous injection of luetin, and it is highly probable that the luetin reaction does not indicate resistance to reinfection or the "lighting up" of a present infection.

Furthermore, I have seen three persons presenting perfectly typical reactions to diphtherin contract diphtheria, and dogs that have reacted to bronchisepticin have contracted canine distemper.

The sum total of these studies indicates that, although antibodies that may be regarded as possessing protective and curative properties toward a certain protein *may* be present in the body fluids of persons and animals hypersensitive to this particular protein, the condition of hypersensitiveness in itself is no direct evidence of their presence or of resistance to a particular infection, although these antibodies are most likely to be present in the body fluids of those persons who are hypersensitive. The positive anaphylactic skin test is therefore, evidence of infection or sensitization to a particular protein without bearing any direct relation to resistance to infection or reinfection.

The clinical significance and practical value of skin reactions are largely of a diagnostic nature for the detection of hypersensitiveness to a protein or proteins which may, when introduced into the organism, produce various acute or chronic lesions and symptoms of disease.

CLINICAL SIGNIFICANCE OF THE SPURIOUS OR NON-SPECIFIC PROTEIN AND TRAUMATIC SKIN REACTIONS.

At the present time the chief clinical significance of the pseudo-anaphylactic and traumatic skin reactions is the likelihood of mistaking them for true anaphylactic reactions.

The Schick toxin reaction for immunity in diphtheria is regarded at present as due to the direct irritant action of diphtheria toxin upon cells at the site of injection; if antitoxin is present in sufficient amount the toxin is neutralized and the inflammatory reaction does not occur. Trauma alone, the preservative, the interaction between protein constituents of the broth and non-specific ferments, or between the protein of autolyzed diphtheria bacilli and specific ferments, may induce a pseudo-reaction which may be mistaken for the true reaction.

It is probable that certain conditions accompanied by an increase of cells and their destruction, as in cancer and pregnancy, may result in the temporary increase of non-specific proteolytic ferments in body fluids and cells, and increase the tendency for the production of pseudo-reactions in the skin. As previously stated, there is also reason to believe that certain diseases accompanied by skin manifestations, as scarlet fever and other exanthemata, increase the tendency to skin reactions.

SUMMARY.

1. Skin reactions may be (a) true or specific anaphylactic reactions; (b) pseudo- or non-specific protein reactions, and (c) traumatic reactions.

2. A non-specific or traumatic skin reaction may occur coincidentally with, or be mistaken for, a true anaphylactic reaction.

3. Intracutaneous skin tests are more delicate than cutaneous tests, but also more likely to yield the non-specific and traumatic reactions.

4. The traumatic and non-specific protein skin reactions may be caused (a) by trauma and the direct injection of an irritant used as a preservative for the material, as phenol, or to a preformed toxic and irritant substance, as diphtheria toxin in the Schick test; (b) to the production of a protein poison of irritant qualities by the action of non-specific proteolytic ferments in the serum or derived from injured cells, upon the protein of the patient's serum, devitalized cells, injected protein, or all three.

5. The true anaphylactic skin reaction, however, is a specific process due to the interaction of specific anaphylactic antibody and specific anaphylactogen, largely within or upon the cells, and with the formation of a diffusible irritant similar to that produced in the non-specific reaction, capable of producing acute hyperemia, edema and leucocytic infiltration of the skin.

6. Certain drugs, as potassium iodide and potassium bromide, increase the non-specific reaction by facilitating the activity of non-specific proteolytic ferments and the production of protein poison, through the removal of anti-ferment; these drugs probably have no direct influence upon the specific anaphylactic reaction.

7. The specific anaphylactic skin reaction is acceptable as a delicate index of hypersensitiveness to a certain foreign protein or proteins, the enteral or parenteral administration of which may be expressed by various lesions and symptoms of disease.

8. The severity of a true anaphylactic skin reaction appears to be an index of the degree of hypersensitiveness.

9. A state of cutaneous anaphylaxis to a particular bacterial protein is not of itself an index of resistance or immunity to the living microparasite, although immunity principles may be coincidentally present with the anaphylactic body.

10. At present the main clinical significance of the non-specific protein skin reaction is the likelihood of mistaking it for a true anaphylactic reaction.

BIBLIOGRAPHY.

1. Sleeswijk, J. G.: Untersuchungen über Serumhypersensibilität. Ztsch. f. Immunitätsf., Jena, Orig., 1909, II, 133-158.
2. Friedberger, E., and Hartoch, O.: Ueber das Verhalten des Komplements bei der aktiven und passiven Anaphylaxie. Ztsch. f. Immunitätsf., Jena, Orig., 1909, III, 581-638.
3. Loeffler, F. C.: Das Komplement als ausschlaggebender Faktor für das Zustandekommen des anaphylaktischen Anfalles. Ztschr. f. Immunitätsf., Jena, Orig., 1910, VIII, 129-144.
4. Friedberger, E. and Hartoch, O.: *Loc. cit.*
5. Nolf, P.: A l'étude des serums antihématiques. Ann. de l'Inst. Pasteur, 1900, XIV, 297-330.
6. Hektoen, L. and Ruediger, G. F.: The antilytic action of salt solutions and other substances. Jour. Infect. Dis., Chic., 1904, I, 379-403.
7. Williams, P. F. and Pearce, R. M.: Abderhalden's Biological Test for Pregnancy. Surg. Gynecol. and Obstet., Chic., 1913, XVI, 411-421.

8. Lange, J. and Larsson, K. O.: Über die Mikrobestimmung einiger Blutbestandteile. Biochem. Ztschr., 1914, LXI, 193-199.
9. Jobling, J. W., Eggstein, A. A. and Petersen, W.: Serum proteases and the mechanism of the Abderhalden reaction. Jour. Exper. Med., 1915, XXI, 239-249.
10. Kolmer, J. A. and Williams, P. F.: A study of the specificity of ferments in pregnancy and the mechanism of the Abderhalden reaction. Amer. Jour. Obstet. and Dis. Women and Child., N. Y., 1915, LXXII, 101-120.
11. Stephan, R.: Die Natur der sogenannten Abwehrfermente. Münch. Med. Wchnschr., 1914, LXI, 801-804.
12. Hauptmann, A.: Das Wesen der Abwehrfermente bei der Abderhaldenschen Reaktion. Münch. Med. Wchnschr., 1914, LXI, 1167-1168.
13. Bettencourt, N. and Menèzes, S.: Les Abwehrferments d'Abderhalden sont réactivables au moyen de l'addition de sérum frais normal. Compt. rend. Soc. de biol., 1914, LXXVII, 162-164.
14. Steisung, Z.: Ueber die natur bei der Abderhaldenschen Reaktion wirksamen Fermentes. Münch. Med. Wchnschr., 1913, LX, 1535-1536.
15. Jobling, J. W. and Petersen, W.: The nature of serum anti-trypsin. Jour. Exper. Med., 1914, XIX, 459-479; *ibid.*, 479-500.
16. Friedberger, E.: Kritik der Theorien über die Anaphylaxie. Ztsch. f. Immunitätsforsch., Jena, Orig., 1909, II, 208-224.
17. Lake, G. C., Osborne, T. B. and Wells, H. G.: The immunological relationship of hordein of barley and gliadin of wheat as shown by the complement fixation, passive anaphylaxis, and precipitin reactions. Jour. Infect. Dis., Chic., 1914, XIV, 364-384.
18. Weil, R.: On the relation between precipitin and sensitizin. Jour. Immunol., Balto., 1916, I, 1-19; *ibid.*, 19-35; *ibid.*, 35-47.
19. Zinsser, H.: Further studies on the identity of precipitins and protein sensitizers (albuminolytins). Jour. Exper. Med., 1913, XVIII, 219-227.
20. Keysser, F. and Wassermann, M.: Über "Toxoepptide." Fol. serol., Leipz., 1911, VII, 593-605.
21. Bordet, J.: Géluse et anaphylatoxine. Compt. rend. Soc. de biol., 1913, LXXIV, 877.
22. Jobling, J. W. and Petersen, W.: *Loc. cit.*
23. Plaut, F.: Ueber Adsorptionerscheinungen bei dem Abderhaldenschen Dialysieverfahren. Münch., Med. Wchnschr., 1914, LXI, 238-241.
24. Peiper, A.: Ueber Adsorptionerscheinungen bei A. R. Deutsche Med. Wchnschr., 1914, XL, 1467-1468.
25. Friedeman, U. and Schonfeld, A.: Zur Theorie der Abderhaldenschen Reaktion. Berl. klin. Wchnschr., 1914, LI, 348-349.
26. Bronfenbrenner, J.: On the clinical value of the serum skin test in tuberculosis. Proc. Soc. Exper. Med. and Biol., N. Y., 1914, XI, 90-92.
27. Bronfenbrenner, J.: Specific Parenteral Digestion and its Relation to the Phenomena of Immunity and anaphylaxis. Jour. Lab. and Clin. Med., 1916, I, 573-584.
28. Friedberger, E. and Girgolauff, S.: Die Bedeutung sessiler Rezeptoren für die Anaphylaxie. Ztsch. f. Immunitätsf., Jena, Orig., 1911, IX, 575-582.
29. Pearce, R. M. and Eisenbrey, A. B.: The physiology of anaphylactic "shock" in the dog. Congr. Amer. Phys. and Surg., 1910, VIII, 402-413.
30. Coca, A. F.: The Site of Reaction in Anaphylactic Shock. Ztschr. f. Immunitätsf., Jena, Orig., 1914, XX, 622-643.
31. Schultz, W. H.: The reaction of smooth muscle of the guinea-pig sensitized with horse serum. Jour. Pharmacol. and Exper. Therap., Balto., 1910, I, 549-569.
32. Dale, H.: The Anaphylactic reaction of plain muscle in the guinea-pig. Jour. Pharmacol. and Exper. Therap., Balto., 1913, IV, 167-223.
33. Weil, R.: A study of the cellular theory by the graphic method. Jour. Med. Research, Bost., 1914, XXX, 87-111.

34. Doerr, R.: *Ergebnisse der Immunitätsforsch.*, Reichhardt, Berlin, 1914, I, 257.
35. Zinsser, H. and Young, S. W.: On the possible importance of colloidal protection in certain phases of the precipitin reaction. *Jour. Exper. Med.*, 1913, XVII, 396-408.
36. Weil, R.: Anaphylatoxin and the mechanism of anaphylaxis. *Proc. Soc. Exper. Biol. and Med.*, N. Y., 1915, XIII, 23 (1087).
37. Kolmer, J. A., Asnis, E. and Freese, A. M.: Experimental studies in tissue ferments. *Proc. Path. Soc. of Phila.*, 1917, 19.
38. Kolmer, J. A. and Moshage, E. L.: A note on the occurrence of pseudoreactions on the skin. *J. A. Med. Assoc.*, Chic., 1915, LXV, 144-146.
39. Engelhorn, E. and Wintz, C. H.: Ueber eine neue Hautreaktion in der Schwangerschaft. *Münch. Med. Wehnschr.*, 1914, LXI, 1115-1116.
40. Falls, F. H. and Bartlett, F. K.: On the specificity of placental proteins in skin reactions of the human body. *Amer. Jour. Obstet.*, N. Y., 1914, LXX, 910-918.
41. Kolmer, J. A. and Williams, P. F.: A study of the specificity of ferments in pregnancy by means of local skin reactions. *Jour. Obstet. and Dis. Women and Child.*, N. Y., 1915, LXXI, 889-910.
42. Stokes, J. H.: Intradermal reactions to emulsions of normal and pathologic skin. *Jour. Infect. Dis.*, Chic., 1916, XVIII, 402-414.
43. Stokes, J. H.: An intradermal reaction to agar and an interpretation of intradermal reactions. *Jour. Infect. Dis.*, Chic., 1916, XVIII, 415-436.
44. Zingher, A.: The pseudoreaction in the Schick test and its control. *Jour. Amer. Med. Assoc.*, Chic., 1916, LXVI, 1617.
45. Doerr, D. and Russ, V. K.: Die anaphylaktische Immunkörper und seine Beziehungen zum Eiweissantigen. *Ztschr. f. Immunitätsf.*, Orig., 1909, III, 181-208.
46. Weil, R.: On the Relation Between Precipitin and Sensitizin. *Jour. Immunol.*, 1916, I, 1-19; *ibid.*, 19-35; *ibid.*, 35-47.
47. Wells C. W.: On the Specific Precipitin in the Blood of Persons Injected with Antidiphtheritic Horse Serum. *Jour. Infect. Dis.*, 1915, XVI, 63-71.
48. Hamburger, F. and Moro, E.: Ueber die biologisch nachweisbaren Veränderungen des menschlichen Blutes nach der Seruminjektion. *Wien. klin. Wehnschr.*, 1903, XVI, 445-447.
49. Sherrick, J. W.: The effect of potassium iodide on the luetin reaction. *Jour. Amer. Med. Assoc.*, Chic., 1915, July 31, 404-406.
50. Kolmer, J. A., Matsunami, T. and Broadwell, S.: The effect of potassium iodide on the luetin reaction. *Jour. Amer. Med. Assoc.*, Chic., 1916, LXVII, 718-719.
51. Kolmer, J. A., Matsunami, T., Immerman, S. and Montgomery, C. M.: The effect of certain drugs upon anaphylactic skin reactions. *Jour. Lab. and Clin. Med.*, 1917, XI, 401-416.
52. Longcope, W. T.: Susceptibility of man to foreign proteins. *Amer. Jour. Med. Sci.*, 1916, CLII, 625-650.
53. Schloss, O. M.: A case of Allergy to Common Foods. *Amer. Jour. Dis. Child.*, Chic., 1912, III, 341-362.
54. Lesné, E. and Richet, C. H.: Anaphylaxie alimentaire aux œufs. *Arch. d. méd. d. infants*, Paris, 1913, XVI, 81-94.
55. Talbot, F. B.: Asthma in Children. Its Relation to Egg Poisoning (Anaphylaxis). *Boston Med. and Surg. Jour.*, 1914, CLXXI, 708-712.
56. Smith, H. L.: Buckwheat Poisoning with report of a case in man. *Arch. Int. Med.*, Chic., 1909, III, 350-359.
57. Strickler, A. and Goldberg, J. M.: Anaphylactic food reactions. *J. Amer. Med. Assoc.*, Chic., 1916, LXVI, 249-252.
58. Blackfan, K. D.: A cutaneous reaction from Proteins in Eczema. *Amer. Jour. Dis. Child.*, Chic., 1916, I, 441-455.
59. Amberg, S.: The cutaneous tricophytin reaction. *Jour. Exper. Med.*, 1910, XII, 435-459.
60. Weil, R.: Serological analysis of a case of serum sickness in a human being. *Proc. Soc. Exper. Med. and Biol.*, 1914, XII, 37-38.
61. Denzer, B. S.: The coexistence of Antibody and Antigen in the body. *Jour. Infect. Dis.*, Chic., 1916, XVIII, 631-647.
62. Force, J. N.: An investigation of the causes of failure in cow-pox vaccination. *Jour. Amer. Med. Assoc.*, Chic., 1914, LXII, 1466.
63. Rosenau, M. J. and Anderson, J. T.: Studies upon Hypersusceptibility and Immunity. *Bull. Hyg. Lab.*, U. S. P. H. and M. H. S., Wash., 1907, No. 36, 7-67.
64. Römer, P. H.: Spezifische überempfindlichkeit und Tuberkuloseimmunität. *Beitr. z. Klinik d. Tuberk.*, 1908, XI, 79-245. (Gives a full bibliography of the earlier literature.)
65. Sata, A.: Immunisierung, Ueberempfindlichkeit und Antikörpersbildung gegen Tuberkulose. *Ztsch. f. Tuberk.*, 1911, XVIII, 1-24.
66. Krause, A. K.: Hypersusceptibility to Tuberculo-protein and its relation to some tuberculous problems. *J. Med. Research*, Boston, 1911, XXIV, 361-409; *ibid.*, 1916, 35, 1-25; 25-43.
67. Austrian, C. R.: The effect of hypersensitiveness to a tubercle protein upon subsequent infection with *Bacillus tuberculosis*. *Bull. Johns Hopkins Hosp.*, Balto., 1913, XXIV, 11-25.
68. Gay, F. P. and Force, J. N.: A skin reaction indicative of immunity against typhoid fever. *Arch. Int. Med.*, Chic., 1914, XIII, 471-479.
69. Gay, F. P. and Claypole, E. J.: An experimental study of methods of prophylactic immunization against typhoid fever. *Arch. Int. Med.*, Chic., 1914, XIV, 671-705.
70. Nichols, H. J.: Observations on antityphoid vaccination. *J. Exper. Med.*, Lancaster, 1915, XXII, 780-793.
71. Doerr, R. and Russ, V. K.: Studien über Anaphylaxie. *Ztsch. f. Immunitätsforsch.*, Jena, Orig., 1909, III, 706-725.
72. Kolmer, J. A. and Berge, J. H.: The relation of the typhoidin skin reaction to immunity in typhoid fever. *Jour. Immunology*, 1916, I, 409-428.
73. Kolmer, J. A. and Broadwell, S.: The relation of the luetin skin reaction to immunity in syphilis, including the treponemidal action of human serum in syphilis. *Jour. Immunology*, 1916, I, 429-442.
74. Kolmer, J. A.: The relation of the diphtherin skin reaction to immunity in diphtheria. *Jour. Immunology*, 1916, I, 443-456.
75. Kolmer, J. A.: An anaphylactic skin reaction to diphtheria bacilli. *Am. Jour. Dis. Child.*, Chic., 1916.
76. Kolmer, J. A., Matsunami, T. and Harkins, M. J.: The relation of the bronchisepticin skin reaction to immunity in canine distemper, including the bactericidal action of dog serum for *B. bronchisepticus*. *Jour. Immunology*, Balto., 1916, I, 571-585.
77. Kolmer, J. A., Harkins, M. J. and Reichel, J.: A cutaneous reaction in canine distemper. *Jour. Immunology*, Balto., 1916, I, 501-511.
78. Noguchi, H.: Personal communication.

DISCUSSION.

DR. KRAUSE: I am sure that we all feel greatly indebted to Dr. Kolmer for coming here to-night and giving us this admirable summary of work that has been done in this extremely involved and difficult field of anaphylaxis.

I think that in any discussion of anaphylaxis we should keep in mind that no one has yet brought forward the proof that anaphylactic shock and the protein intoxication which manifests itself by symptoms that we generally call serum sickness are dependent on the same factors as the inflammation by which cutaneous hypersensitiveness expresses itself. I prefer to use the term anaphylaxis or anaphylactic shock to indicate the first condition, and cutaneous hypersensitiveness for the latter; and from the known facts at hand I cannot admit that the two reactions are the same, though in his paper Dr. Kolmer stated that it is generally agreed that they are identical.

Anyone who works in tuberculosis will soon learn that the conditions which will sensitize an animal in an anaphylactic sense will not necessarily sensitize its skin, and, that to bring about cutaneous hypersensitiveness, certain very definite and strict requirements must be fulfilled. It is the easiest thing in the world to sensitize a normal animal with tuberculo-protein so that subsequent intravenous or post-orbital injections of the protein will produce anaphylaxis. But an animal thus treated will not acquire skin hypersensitiveness. To attain this the animal must have a focus of infection (Römer, Baldwin, Hamburger, Krause). In no other way than by the introduction of bacilli and the consequent production of foci has anybody thus far succeeded in sensitizing an animal's skin. The mere parenteral injection of tuberculo-protein in any form—soluble or insoluble—will, however, render an animal anaphylactically sensitive.

After a number of years of work I could never determine that mere anaphylactic sensitiveness conferred any immunity upon an animal against bacillary invasion. An animal during the period of anaphylactic shock, and before it has completely recovered from the symptoms, will often strike one as being less resistant to infection. But in the period during which it is merely hypersensitive to protein, one can detect no alteration in its resistance.

The story is very different, however, once its skin (and other tissues) are hypersensitive. Skin (tissue) hypersensitiveness and immunity to infection (re-infection) occur under exactly the same conditions so far as we know: and it is not improbable that one is a function of the other. Skin or tissue hypersensitiveness expresses itself by the capacity of the skin or tissue to react in an inflammatory manner whenever the proper protein is applied *in situ*. The same inflammation will occur in the skin of a sensitive animal if the proper living bacilli are locally injected. We might therefore conceive that perhaps this inflammation occurring rapidly only in the sensitive animal after the implantation

of living bacilli has a good deal to do in hemming in the bacilli and preventing their invasion of the organism. We might then consider that immunity to infection is in some way or other bound up in the inflammation by which a sensitive animal reacts.

As a matter of fact the tuberculous animal is both hypersensitive (skin or tissue) and immune. This hypersensitiveness and immunity both reach their maximum once a certain stage of activity of the disease is established. As the disease heals, both the hypersensitiveness and the immunity tend to diminish. Anaphylactic hypersensitiveness is not bound by these rules in tuberculosis.

It is not improbable too that the wide diversity of lesion met with in tuberculous involvement is largely determined by the variation in tissue hypersensitiveness at the particular time of bacillary implantation. The tuberculous pneumonias, the collateral inflammations, the oedema, the hæmorrhagic tissue reactions, the effusions into serous cavities are all expressions of local tissue hypersensitiveness produced by previous infection of the animal. I have never seen a normal animal react *immediately* to a first infection with tubercle bacilli in any other way than focally. But if the animal is already tuberculous, in other words, is already hypersensitive and relatively immune, then we shall find every kind of exudative or inflammatory reaction following re-infection: and the intensity and extent of the tissue alteration are determined by the degree of tissue hypersensitiveness on the one hand, and, on the other, by the number of bacilli brought to bear at any given point. In other words, the nature of the pathological change depends to a certain extent on the immune reactions of the tissues. I can think of no work that would promise more fruitful results than a rejuvenescence of the study of pathological anatomy in infectious disease, if the study were a comparative one and the diseases were studied developmentally. We should surely go far if we compared under natural and immune conditions the tissue response to irritation by micro-organisms, which, though related, are known to produce different effects.

TUBERCULOSIS OF THE TONGUE. SPECIFIC CURE.

By WM. CHARLES WHITE, M. D., and C. HOWARD MARCY, M. D.

(From the R. B. Mellon Research Laboratory, Tuberculosis League of Pittsburgh.)

An excellent paper on Tuberculosis of the Tongue by J. R. Scott¹ has recently appeared during the preparation of this report.

It is unnecessary to cover again the historical side of this field; reference to Dr. Scott's paper will answer every purpose in this regard.

A case has just come under our care presenting unusual features. The patient was under our constant supervision for advanced pulmonary tuberculosis for two years, prior to the advent of the lingual tuberculous ulcer which is reported here.

W. E., aged 30 years, applied at the hospital for care in June, 1914. At this time the family and personal histories were negative up to the time of his immediate illness, save for two attacks of pleurisy, one in 1906 and one in 1913. There was no remaining evidence of these attacks on physical examination during his stay in the hospital.

His tuberculosis had begun with cough and sputum three years before. His chief complaints on admission were cough, sputum, loss of weight, shortness of breath and sometimes pain

on deep breathing. He had been at Mt. Alto, a state institution, without improvement, for six months prior to his admission to the Tuberculosis League Institution.

The physical examination on admission revealed signs of advanced tuberculosis of the lungs, involving both upper lobes completely and the lower lobes on both sides to the tip of the scapula. Cavitation was doubtful in the apex of the left lower lobe opposite the fourth and fifth dorsal spines. The sputum amounted to about 10 c. c. in 24 hours, and ranged in tubercle bacilli content from No. ii to No. vii (Gaffky). These were mostly long, slender, and beaded forms. His urine was normal, his Wassermann reaction negative. His blood examination: Hb., 90%; R. B. C., 5,800,000; W. B. C., 7800; diff. count: lymphocytes, 23.6%; large mono., 1.5%; trans., 3.40%; poly., 67%; eosinophiles, 3.5%; mast cells, 1%. His skin sensitiveness to O. T. was represented by no reaction to 1/100 c. c. of .25%, 1% and 2% solutions, but there was a positive reaction of 3 x 3 mm. to 1/100 c. c. of a 4% solution. On the basis of this reaction, he was given .00004 gm. of O. T.



FIG. 1.—Appearance of tuberculous ulcer of the tongue before treatment with tuberculin. This ulcer had persisted for six months.



FIG. 2.—Appearance of the same ulcer after four injections of .008 gm. O. T.

intradermally, in accordance with a method of dosage before described by us.² With this dose he gave an intracutaneous reaction of 2 x 2.5 cm. at the site of the injection dose. This dose was given for some time, then gradually increased in size over a period of 11 months, as he gained in weight and well-being. The sensitiveness had so far disappeared that on discharge, in May, 1915, he was receiving .009 gm. of O. T. In May, 1915, he was discharged and went home. He was greatly improved, having gained 17 pounds in weight and reached four hours' exercise (mainly walking) in 24 hours. He still had about 2 c. c. of sputum with a tubercle bacilli content represented by Gaffky ii. He took up light work, collecting and giving clerical assistance intermittently, as he could obtain it. He continued his tuberculin in the dosage last mentioned, and remained comparatively well till November, 1915.

In November, 1915, he noticed two small painless nodules developing on his tongue. These later broke down and developed an ulcer with a yellowish discharge. The chief symptoms of the ulcer were soreness and swelling. The pain was so severe when food was taken that the patient could not eat. He lost in five months 20 pounds. His home physician, Dr. Leydic, of Tarentum, treated the ulcer locally with silver nitrate and iodine for five months. In March, 1916, Dr. Leydic sent him again to the hospital. On admission, the lung lesion had not increased in area but was discharging more sputum. The whole amount was now 15 c. c. in 24 hours. The t. b. content was represented by Gaffky viii. The Wassermann reaction was negative. The blood examination showed: Hb., 90%; R. B. C., 6,470,000; W. B. C., 12,800; poly., 64.6%; lymphocytes, 28.2%; large mono., 6%; trans., 1.6%; eosinophiles, .6%. The high red blood cell count was probably due to his inability to take fluids, owing to the pain produced by swallowing and by taking into the mouth substances varying from the mouth temperature.

In addition an ulcer was found on the upper surface of the tongue 1.5 cm. in diameter, 2 cm. from the tip, confined to the right of the middle line. He was readmitted to the hospital.

Only by the use of cocaine locally was he able to eat. He lost 10 pounds in weight in two months in the hospital, and the ulcer continued to increase in size.

In April, Dr. Sieber removed a section of the ulcer. This was sectioned and examined by Dr. Bruecken and Dr. MacLachlan of the Department of Pathology of the University of Pittsburgh, and the diagnosis of tuberculous ulcer with giant cells and tubercle bacilli in the tissue was rendered.

The surgeon's advice was to excise the tongue wide of the lesion. In view of the fact that tuberculin had been given intradermally and had neither prevented nor cured the local infection in the tongue, its further use was considered as of no value. However, on account of some good results we had had with lupus, by injecting tuberculin into the base of the lupoid patch, we suggested that a trial be given to injection of tuberculin into the base of the lingual ulcer.

His skin sensitiveness was again taken, and his dose was found to be (by the method formerly described by us) .008 gm. of O. T. On May 4 this dose of old tuberculin was injected,

from the side of the tongue, through the muscle substance, so as to infiltrate the base of the ulcer, with a long, fine hypodermic needle. At the end of 24 hours the tongue was swollen, red and a little more painful. At the end of 48 hours it was still slightly swollen, but not sore, and the increased redness was fading. After this the ulcer commenced to diminish in size, until at the end of one week it was not more than half the size and the patient was able to eat without pain.

On May 18 a second dose of O. T. was given in the same way, with a similar reaction and result, and one week later a reduction again of approximately 50% in the size of the ulcer.

On June 1 the same dose was given into the tongue. On June 2 he was discharged and returned to his home. On June 12 he returned again to the dispensary; at this time the ulcer had almost completely healed and he was again rapidly improving in weight and health. His last dose of tuberculin was given in July, when the ulcer was quite healed, and only a small fissure left to mark its former site.

Any explanation of the action of tuberculin in this case must be purely theoretical.

The patient had had far advanced tuberculosis of both lungs, which had healed with a large amount of fibrosis, and had left him afebrile and with a fair working ability. This may be taken as an indication of a great resistance, and that he had within his body somewhere, probably in his circulating fluids, substances which could be expressed in terms of tubercle bacillus resistance, if we had any means of isolating or measuring them.

On the one hand, there may be certain lytic substances in the circulating fluids in individuals who are improving from tuberculosis, but the structure of the tubercle devoid of blood-vessels may allow none of these to reach the central portion of the tubercle where the tubercle bacilli lie. The specific reaction to tuberculin, producing as it does a focal inflammation, may, by the accompanying swelling due to increased exudation, press apart the various cells packed around the individual tubercles and admit to the center of the tubercles any tubercle-bacilli-destroying substance present in the circulating fluids. This seems to us the most logical explanation.

On the other hand, it may be contended that all the inflammation does is to stimulate the production of mesoblastic cells at the periphery of the tubercle; that these later secrete fibrils which by contraction destroy the focus of the disease. The rapid cure which resulted in this case, after so long a persistence, makes the former contention more reasonable, as sufficient formation of new fibrous tissue could scarcely occur in four or five days after injection of the tuberculin to produce such reduction as occurred in the size of the ulcer. It is more likely that the diminution in size followed coincidentally with the destruction of the etiological factor, that is, the tubercle bacilli.

If this procedure seems justified by further study, localized tuberculosis conditions can undoubtedly be very materially aided by this form of treatment. It seems especially applicable to local lesions in the laryngeal region and might safely be tried by those skilled in laryngoscopy.

It is not felt that we have reported any new procedure. The principle involved is probably the same which Dr. Trudeau found by specific treatment with tuberculin in curing tuberculous lesions in his rabbits' eyes.

Surely such a procedure is infinitely better in localized tuberculosis, such as the tongue lesion, than treatment by excision. The rapid cure after the long persistence in this case left no doubt about the influence of the specific agent.

NOTE.—Since this paper was written, the patient has returned with another tuberculous mass a little distance away from this in the tongue and this has been cured by two injections of tuberculin in a way similar to that described in this paper.

REFERENCES.

1. Scott: American Journal of the Medical Sciences. Sept., 1916, CLII, No. 3, 411.
2. White and Van Norman: Archives of Internal Medicine. Oct., 1910, VI, 449-468.

ABSTRACTS OF PAPERS

Representing Work Done in The Johns Hopkins Hospital, but Published or to be Published Elsewhere than in the Bulletin.
Prepared by the Authors.

DOUBLE URETER AND KIDNEY, WITH CALCULOUS PYONEPHROSIS OF ONE-HALF; CURE BY RESECTION. THE EMBRYOLOGY AND SURGERY OF DOUBLE URETER AND KIDNEY.

By HUGH H. YOUNG and EDWIN G. DAVIS.

(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore.)

(Abstract from the Journal of Urology, 1917, I, 17.)

During recent years we have had in our clinic several cases of double kidney and ureter in which one portion of the double kidney was diseased. The present case is the only one of these which has come to operation, and is unique in that it is the only one of its kind to be found fully reported in the literature. The upper calculous pyonephrotic portion of a left double kidney with bifid ureter was diagnosed by means of pyelography, and the diseased portion was successfully resected, the lower normal portion being left *in situ* with an undisturbed blood supply and ureter. The patient, a man of 57, was admitted on April 7, 1916, to the James Buchanan Brady Urological Institute, complaining of a pain in the left flank. The pain was dull and aching in character, was increased by exertion; it had been present, with exacerbations and remissions, for 10 years. There was no history of any attack resembling renal colic. He complained also of frequency of urination, and the urinary examination showed a marked pyuria. The pyelogram showed on the left side a double renal pelvis with bifurcation of the ureter at the level of the third lumbar vertebra, and about 9 cm. below the lower pelvis. A large branching calculus completely filled the upper larger pelvis. There was no apparent abnormality of the right pyelogram. At operation (Young), a slight but distinct furrow was found demarcating the two kidney segments, and at this level it was possible to resect the upper portion, controlling a moderate amount of bleeding by mattress sutures through the upper pole of the normal portion. Convalescence was uneventful. The patient's symptoms (pain in the back and frequency of urination) were entirely relieved, and it was later demonstrated that the half kidney secreted normal, pus-free urine containing as much as 5 per cent phenolsulphonaphthalein in one-half hour.

As to the embryology of bifid ureter, there is a general agreement among authors that this form of anomaly (bifid

ureter or incomplete double ureter) may be accounted for by a premature or exaggerated bifurcation of the tip of the ureteral bud, the split extending varying distances down the ureteral stalk instead of being confined to the bulbous tip or primitive pelvis. This bifurcation normally takes place to a limited extent. The ureter first appears (in an embryo of about 5 mm.) as a budding or evagination from the Wolffian duct, close to the opening of the latter into the cloaca. The tip of the bud becomes bulbous as early as the 6.6 mm. stage, the primitive pelvis thus becoming differentiated from its more slender stalk, the future ureter, and as early as the 8 mm. stage a bifurcation of the primitive pelvis has taken place, separating it into upper and lower divisions, the first evidence of the calices. It may readily be understood that, if this normal bifurcation or splitting of the primitive pelvis should be excessive and extend down the ureteral stalk, two separate pelvis and a bifid ureter would be produced. Felix describes this as a "precocious splitting of the ureter," the bifurcation taking place before the formation of the primitive renal pelvis, and the two ureters thus formed descending parallel to one another. He designates such forms of ureter as "cleft ureter," reserving the term "double ureter" only for those that have separate openings in the bladder. Complete double ureter is considered to be formed either as the result of two separate evaginations from the Wolffian duct, or as the result of the process of dilatation of the lower end of the Wolffian duct (and of the uncleft lower end of the ureter) by which the former comes to form a part of the bladder wall.

A complete survey of the literature shows that ureteral duplication is surprisingly common, especially in autopsy records, and occurs much more frequently than all the other forms of gross renal anomaly taken together. An average of the estimates of various observers places the frequency of this anomaly at about 3 per cent of all individuals. In the surgical literature, however, reports of bifid ureter and double kidney are quite rare. We were able to find only 26 case reports in which this form of anomalous kidney was explored surgically. In two of these the operation was undertaken merely on account of the incontinence produced by the supernumerary ureter opening externally (in the vagina), there being no lesion in the kidney itself, and in six cases the operation was nephrotomy. The remaining 20 operations upon double

kidneys were all nephrectomies, and in all but one (Albarran) the operation was complete nephrectomy. In the case reports of 16 of these nephrectomies it was definitely stated that half of the excised kidney was normal, and these 16 would therefore have afforded an opportunity for partial nephrectomy with preservation of a normal portion. Of the 20 nephrectomies the diagnosis of ureteral duplicity was made before operation in two instances only; in 18 the condition was accidentally discovered during the course of the operation, or later by an examination of the pathological specimen. There remains the case of Albarran, the only one in the series in which the normal portion of the kidney was preserved. Albarran, however, merely briefly mentioned his case in the transactions of the Association Française d'Urologie (1905), and has made no official report. It is of interest to note that, out of 24 cases of double kidney showing a pathological process in one segment, in 19 (practically 80 per cent) the upper segment was involved. In view of this uneven percentage it is fair to assume that partial obstruction of the superior ureter, due to its position with respect to the lower kidney segment and to the kidney pedicle, had been an important factor in producing disease.

CONCLUSIONS.

The case reported above is apparently unique in that it is the only such case to be found fully reported in the literature.

The condition of double kidney and ureter is not rare, and the upper half is most often the seat of disease; its surgical importance is therefore great.

The advent of ureteral catheterization, radiography and pyelography has made the diagnosis easy and we should expect the discovery of more cases in the future.

The radical cure by excision of the diseased half of the kidney with its pelvis and ureter is undoubtedly the method of choice.

THE EFFECT OF CALCIUM, WATER, AND OTHER SUBSTANCES GIVEN INTRAVENOUSLY, ON BLOOD COMPOSITION AND URINARY SECRETION.

By DAVID M. DAVIS.

(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore.)

(Abstract of article in Journal of Urology, 1917, I, 113.)

In attempting to restudy the relation between blood composition and urinary secretion the effort has been made to inject quantities of fluid intravenously in such a way as to produce no diuresis. The changes in blood composition occurring under these conditions can then be determined.

Three procedures were utilized. In the first, distilled water; in the second, solutions of Ca, or of mixtures of Ca and Na chlorides; in the third, weak solutions of dextrose were injected.

It has long been known that distilled water given intravenously causes no diuresis. J. B. MacCallum concluded that calcium exercises an inhibitory effect on urinary secretion, though this has been denied by others. Woodyatt, by the use

of an automatic pump, was able to prove that, if dextrose is given a dog at a rate of less than 0.85 gm. per kilogram-hour, no glycosuria or diuresis occurs.

All the injections were made at constant rates over considerable periods of time, using a pump similar to Woodyatt's. Determinations were made while the injections were going on.

With distilled water, no diuresis was observed. The water content of the blood, however, increased 2 per cent, while the Δ of the blood fell 0.057°.

It was thought that Ca would probably decrease urinary secretion, since its biological actions are so generally antagonistic to those of Na. The observations of MacCallum were confirmed, the urine output being decreased. Where large doses of Ca solution were used, the hemoglobin percentage rose and the water content of the blood fell very markedly. The Δ , however, remained constant, showing that a large quantity of isotonic fluid had gone to the tissues from the circulation. In other cases where Na was added to the Ca solutions and the amount of Ca reduced, the blood water content was less affected, showing slight increases, while Δ showed slight decreases. In these cases, the urinary secretion showed no, or slight, augmentation. A further experiment with kymograph record showed that these mixed Ca and Na solutions do not depress the general blood pressure.

When dextrose solutions were injected, at rates of 0.65 and 0.7 gm. per kilogram-hour, the blood water and blood sugar were increased, while Δ showed a moderate fall. One experiment showed diuresis during the second hour—evidently a subnormal tolerance.

Thompson, in an article published in 1900, has drawn conclusions concerning the mechanism of diuresis which there has been little reason to change since. According to him the diuresis, as measured by the quantity of urine secreted, does not run parallel to the blood pressure, the kidney volume, or the amount of hydremia.

Changes in the blood flow through the kidney have had ardent advocates for this important rôle. Löwi, using an extraordinary method, namely, the observation of the color of the venous blood as it emerged from the kidney, came to the conclusion that every diuresis is accompanied by an increased flow of blood. Such an inexact method does not invite great confidence, but Löwi is undoubtedly correct in supporting Thompson in his attack on the oncometric method as an index of blood flow in the kidney. Löwi enclosed the kidney in a plaster cast, making expansion impossible, yet with diuretics there was observed the change in color of the renal vein, to arterial red, that he associated with increased flow. Bunch demonstrated this in the most conclusive manner for the salivary gland, using an air plethysmograph and actually measuring the blood coming from the vein. Stimulation of the chorda tympani gave an increase in the blood flow with simultaneously increased secretion, but with a contraction of the gland. Histological studies of the kidney make it apparent that the renal epithelial cells vary greatly in size under different conditions.

It seems that one must conclude that diuresis can occur independently of changes in the blood flow. It is difficult to conceive how changes in the vascular bed, at most changes of 100 per cent or so, can cause increases in urinary secretion amounting to 10,000 per cent or more of the normal, if blood composition is constant or the changes in it are of no importance. In addition, changes in blood composition, as has been seen, do occur. The writer believes, therefore, that the burden of proof should rest on those who claim that blood composition is of less importance in diuresis than renal blood flow.

The older writers lay great stress on the concentration of the urine, especially in relation to that of the blood (Frey). It has, however, been demonstrated that the excretion of various substances reaches its maximum at a different time from that at which the diuresis is greatest, and from this viewpoint it is much more convenient to assume that each urinary constituent, including water, has its own excretory mechanism, partially and probably in large degree independent of the others. The total molecular concentration of the urine would then be only an accidental resultant from the action of these mechanisms. It can then be further assumed with Magnus that an increase in the concentration of any constituent will cause its excretion in increased amount, and with Sollmann that the constituents of the blood provide the normal stimulus to renal activity. It is immediately apparent that the independence of the mechanism is not absolute, since one so seldom obtains a great increase in any constituent in the urine without a simultaneous increase in the water, although it is of course possible to do so, especially with certain constituents. Water occupies a peculiar position among urinary constituents, since its presence in the renal secretion is necessary not only to relieve the body of an excess, but also to act as a solvent for all the other constituents. It is suggested, therefore, that the mechanism by which so many salts produce a hydremia is a very necessary one for this purpose. It complicates the picture greatly, however, when explanations are attempted, especially since it makes the content of the body in water and other substances beforehand so important. That this has much influence on diuresis has been shown by Haake and Spiro.

But it is further suggested as an amplification of the theory of Magnus that, conversely, a decrease in the concentration of any urinary constituent in the blood tends to decrease renal activity and may serve to counteract the effect of a simultaneous increase in some other constituent. Thus, the simple addition of water to the blood would always bring about such a counteraction by simply diluting the blood, if not compensated in some way, and the bare statement that water given intravenously is not a diuretic scarcely affords an adequate explanation of the situation. Further, any procedure which caused any substance to leave the blood for the tissues would indirectly diminish urinary secretion.

It is felt that the experiments in this paper offer some support for this suggestion. The regulatory mechanism of the tissues is evident in the injection of hypotonic NaCl solution, where the chloride and molecular concentration of the

blood is kept up to normal, while a hydremia develops, evidently at the expense of the colloid constituents of the plasma, and indicating, therefore, almost surely an increase in blood volume.

SUMMARY.

1. Injections of fluid in considerable amounts have been made intravenously in dogs, according to three methods, without producing diuresis.
2. In such cases definite hydremia and definite hyperglycemia may be present without diuresis.
3. Where hydremia occurs without diuresis, there has usually been a definite decrease in the molecular concentration of plasma, as shown by the depression of the freezing point (Δ).
4. Solutions of calcium chloride given intravenously cause the urinary secretion to diminish, and in addition precipitate a great loss of water from the blood to the tissues. Given with sodium chloride, calcium chloride will antagonize the diuretic effect of sodium chloride. In such a case, the general blood pressure is not changed.
5. Various observations upon current theories of urinary secretion and additions thereto have been made.

A MODIFIED WOODYATT PUMP.

By D. M. DAVIS and W. S. GORTON.

(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore.)

(Abstract from the Journal of Urology, 1917, I.)

The authors describe a simplified and less expensive form of an electric pump devised by Woodyatt. The mechanism actuates a Record syringe, and serves to make intravenous injections over long periods of time at predetermined and constant rates.

STUDIES ON THE GROWTH OF CELLS.

CULTIVATION OF BLADDER AND PROSTATIC TUMORS OUTSIDE THE BODY.

By MONTROSE T. BURROWS, J. EDWARD BURNS and YOSHIO SUZUKI.

(From the Departments of Pathology and the James Buchanan Brady Urological Institute, Department of Urology, The Johns Hopkins University, Baltimore, Md.)

(Abstract from the Journal of Urology, 1917, I, 3.)

Up to the present time no attempt has been made to cultivate bladder or prostatic tumors *in vitro*. Thinking that a study of this kind might aid in a better understanding of the clinical and pathological properties of these tumors, and that these tissues would possibly show peculiarities in their reactions which might aid in a better understanding of the growth of cells in general, we undertook this study.

Evidence had already been found which indicated that tissue cells were not highly organized elements. They are probably unable to utilize the food materials of the medium. Their growth depends upon the presence of specific substances. In the cultures these specific substances are liberated by the cells

within the fragment. A growth in the cultures is a simple transfer of materials from the cells within the fragment or, in a less favorable environment, to those on the periphery or those which migrate into the medium. Further growth in these cultures takes place only along surfaces. In many of the plasma cultures the cells grow along the surface of the fibrin. Measurements have shown that those cells which grow actively and divide by mitosis are not, however, directly in contact with the fibrin surface.

Human tissues liquefy the plasma clot, and the cellular activity is observed only in a small percentage of the culture. It is known that tissues of chick embryos and the embryos of several other animals, as well as certain malignant tumors, may grow in layers of liquid media, isotonic NaCl solution, Ringer's solution, serum, etc. In these media the cells grow in a plane near the free surface of the media or near the surface of the cover-glass over which the medium is spread. This has made it seem evident that the medium previous to the growth of the cells must have become covered with a layer of substance which was fluid in nature and had flowed out over the surface. In the cases where simple salt solutions were used as media, this substance must have come from the tissue fragment.

In the cultures of chick tissues it was often difficult to absolutely demonstrate the existence of such substances.

We have studied the culture of 12 tumors of the bladder and prostate. The method used consists in brief in placing small fragments of tumor tissue (1 mm. in diameter) in a layer of media (5 to 10 mm. in thickness) on the surface of a cover-glass, inverting over this a hollow ground slide, and sealing it in place with vaseline and paraffin. The cultures thus prepared were incubated at 37° C.

The media used have been prepared plasmata from the blood of patients from which the tumor was removed, plasmata from the blood of normal individuals and a medium consisting of agar, .25 per cent, dissolved in isotonic NaCl solution, or isotonic NaCl solution and acetic fluid. No difference was noted in the cellular activities of the cultures whether the plasma used as medium was obtained from the first or second source. The activity was as great in the agar medium as in the plasma.

Of the 12 tumors used for these cultures, seven were clinically malignant bladder papillomata; one was a benign bladder tumor, two were cases of benign hypertrophy of the prostate and two were prostatic tumors, each of which showed in one portion typically benign hypertrophy, the other part having undergone carcinomatous change. Besides these, one series of normal bladder epithelium was also tested. Cellular activity was observed about the fragments of all of the malignant tumors excepting two. One, a bladder tumor, which had been removed after an application of a strong solution of cocaine, and the other, a malignant cancer of the prostate, which had been treated for four months with radium. No cellular activity was noted about the fragments of normal bladder epithelium, about any of the fragments of the benign tumors, or the benign portions of those prostatic tumors which showed local areas of carcinomatous change.

The plasma clots were liquefied around all the fragments of tissue studied. This was not only true of the first culture, but it occurred again if the fragments were transplanted to fresh plasma medium after 24 hours. The cellular activity took place in a liquid medium. In these cultures it was possible to see a membrane form over the surface of a medium. It formed always previous to the growth of the cell. No membranes formed about the fragments of normal epithelium, or the fragments of the benign tumors. The membranes that formed about the fragments of malignant tumors contained a large number of granules which made them easily seen. A sharp line of demarcation between them and the underlying medium was not made out. The surface of the medium which they covered was held fixed and could not be disturbed easily by shaking. The cells migrated in a plane just beneath this membrane.

These observations have shown several facts of interest: First, that the diffusion of a substance, or certain substances, from the tissue fragment over the surface of the medium to form a membrane was essential for the activity of the cells; second, the cells move in contact with the surface of this membrane; third, that such a diffusion and cellular activity are observed only about the fragments of the definitely malignant tumor; fourth, there was no diffusion of such substances or cellular activity noted demonstrable about the fragments of one of the malignant tumors which had been treated for four months previously with radium. These last facts indicate that this method may be important in determining the malignancy, following the course of treatment and studying the biological properties of these tumors.

THE RELATION OF THE NON-PROTEIN NITROGEN TO THE UREA NITROGEN OF THE BLOOD.

By HERMAN O. MOSENTHAL and ALMA HILLER.

(From the Medical Clinic of The Johns Hopkins Hospital.)

(Abstract of article appearing in the Journal of Urology, 1917, I, 75.)

Considering all the cases studied, it is apparent that as the non-protein nitrogen of the blood rises it is accompanied by a disproportionately rapid increase in the urea. This is expressed in the upward trend of the percentage figures for the urea nitrogen of the total non-protein nitrogen.

The conclusions which may be drawn from a closer analysis of these statistics are as follows:

In chronic nephritis, not complicated by myocardial insufficiency or uremia, the relation of the urea nitrogen to the total non-protein nitrogen of the blood shows that the urea increases faster than the non-protein nitrogen, the increase being very similar to that which is found when all the cases are averaged, and presenting no special characteristics.

In cases of nephritis complicated by uremia, the percentage of urea nitrogen has a tendency to be higher than in any other class of cases. Especially noteworthy is the value of 75 to 80 per cent in cases in which the non-protein nitrogen of the blood is 40 mg. per 100 c. c. or less.

Cases of myocardial insufficiency show a marked rise in the percentage of urea nitrogen in those rather rare instances when the non-protein nitrogen increases in the blood beyond the normal of 30 mg. per 100 c. c.

Patients suffering with chronic nephritis complicated by myocardial insufficiency accumulate urea more rapidly in proportion to the other non-protein nitrogenous constituents of the blood than do the cases of chronic nephritis not associated with myocardial insufficiency.

Cases with acute nephritis exhibit a decidedly higher percentage of urea nitrogen than do the instances of chronic nephritis.

The cases with a high non-protein nitrogen in the blood, not included in the previous groups, have a lower proportion of urea nitrogen to the total non-protein nitrogen of the blood than those afflicted with uremia, and they approximate the figures given for chronic nephritis.

Many patients with a normal total non-protein nitrogen of the blood—that is, less than 30 mg. per 100 c. c., show a higher proportion of urea nitrogen than the normal of 50 per cent, though their clinical condition would indicate no renal involvement. The proportionately higher quantity of urea found in the blood of these individuals is believed to demonstrate a depression of renal function.

In acute renal disease, followed by improvement, the percentage of urea nitrogen in the blood may rise and again return to the normal of 50 per cent or less, thus reflecting the progress of the condition.

The relation of the urea nitrogen to the total non-protein nitrogen exhibits a tendency to remain unchanged in each patient. Thus, three cases of chronic nephritis over considerable periods showed a fairly constant concentration of urea nitrogen at a normal level of 50 per cent or less, at a level of 65 per cent, and at 70 to 80 per cent, respectively. This moderate fixation is not to be accounted for by unvarying values of the total non-protein nitrogen, for in each patient these fluctuated widely. The protein katabolism and anabolism may result in exceedingly marked loss or retention of nitrogen, which at times may be reflected in the level of the total non-protein nitrogen and urea nitrogen of the blood, at others, not; in spite of this, the percentage of urea nitrogen remains fairly constant.

It is tempting to assume that the metabolic activities of the tissues through increased protein breakdown may also be responsible for part of the picture. However, when cases are examined in which there is retention of nitrogen due to renal insufficiency alone, not complicated by changes in the other tissues of the body, the same high percentage of urea nitrogen is demonstrated. Polycystic disease of the kidney represents such a condition. In this disease, the same increase in the percentage of the urea nitrogen in the blood as in the instances of nephritis was demonstrated. After nephrectomy in a dog, which may be regarded as an example of maximal uncomplicated renal insufficiency, the percentage of urea nitrogen rapidly rose as high as 86 per cent, and remained in this neighborhood until death supervened.

Taking these facts into consideration, it would seem that ordinarily when protein material is metabolized, approximately 80 per cent of the nitrogen passes into the blood in the form of urea, which is the percentage of urea nitrogen found in the normal urine. Kidneys whose function is not involved maintain the percentage of urea nitrogen of the total non-protein nitrogen at a level of 50 per cent or less in the blood. As the kidneys become inefficient, their impairment of function is recorded in a rise of the percentage of urea nitrogen.

STUDIES ON THE METABOLISM OF CELLS IN VITRO.

I. THE TOXICITY OF α -AMINO-ACIDS FOR EMBRYONIC CHICKEN CELLS.

By MONTROSE T. BURROWS and CLARENCE A. NEYMANN.

(From the Pathological Laboratory and the Laboratory of Internal Medicine, Henry Phipps Psychiatric Clinic, The Johns Hopkins University, Baltimore, Md.)

(Abstract from Journal Exp. Med., Jan. 1, 1917, XXV, No. 1, pp. 93-108.)

The observations recorded were noted during a series of studies directed towards finding an artificial medium for cultivating cells *in vitro*. In the tissue culture the nutrient materials for the growing cells are derived from the cells disintegrating in the center of the fragment of tissue. The culture reaction is none other than a transfer of material from these cells in a less favorable environment to the growing cells on the periphery of the fragment which are in a more favorable environment. Previous evidence had given rise to the belief that the body cells are fluid-like structures. In the cultures they are unable to break down complex substances and to build the products thus liberated into their own protoplasm. Cell growth is a reaction between the cell and a specifically organized mechanical and chemical environment. It is a differential surface tension reaction. There is a definite period for the growth of cells about a given fragment which has been placed in a medium of blood plasma. Transplanting the fragments every three days, we can thus predict the number of transplants in which growth will take place before the cells become exhausted. The number of transplants differ with different tissues.

We observed the effect on the cells of the addition of carbohydrates, fats, peptones and α -amino-acids to the medium. Fragments of heart muscle and skin of chick embryos and foetal chickens were the tissues used. They were planted in plasma, prepared from the blood of adult chicken. The addition of carbohydrates and fats caused no change in the growth activity, which is of present interest. The addition of a 2.5 per cent isotonic solution of peptones prepared from the yolk of eggs did not in any way effect the growth. The addition of an isotonic solution of a mixture of α -amino-acids, prepared by hydrolizing egg yolk proved toxic. Fearing this toxicity might be due to the method of preparation, we tried the addition of isotonic solutions of the individual α -amino-acids. These also proved to be toxic when used in certain concentrations. The cells of young embryos were killed after

a few days' growth in the first culture. The cells of the older embryos and foetal chickens were more resistant, but they were also killed after a few transplants. Lower dilutions inhibited the growth and eventually killed. At first, however, they showed slight stimulation. This was a functional rather than a growth stimulation; it was seen only in those cultures in which fragments of heart muscle had been used. This stimulation was noted by the active contraction of the fragments.

FURTHER OBSERVATIONS ON THE USE OF THORIUM IN PYELOGRAPHY.

By J. EDWARD BURNS.

(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Md.)

(Abstract from the Journal of the American Medical Association, 1917, LXVIII, 533.)

Since the publication of the preliminary report on the use of thorium solution as a pyelographic agent, many experimental investigations as to its pharmacologic action and much clinical evidence after its employment in 185 cases have led to the conclusion that it fulfills all the conditions requisite

for an ideal pyelographic medium. It is non-toxic (within the ordinary limits of usage), non-irritating, opaque to the Roentgen Ray, giving a splendid outline of renal pelvis and ureter and is inexpensive, being about one-third the cost of collargol. The solution contains the double citrate of thorium and sodium, sodium citrate and sodium nitrate. It is a clear, watery solution (therefore perfectly clean) which is not bactericidal, and should therefore be sterilized before being used. For pyelograms, the 15 per cent solution should be used, and for cystograms the 10 per cent solution. The gravity method should always be employed in the introduction of the solution into the renal pelvis and ureter. Great care should be exercised in making pyelograms in cases where there is marked impairment of renal function, for in such cases the introduction of any solution into the renal pelvis might so disturb the already markedly impaired functional activity of the kidneys as to cause the onset of uremia. This solution, either by its adhesive properties, by its capability of being absorbed, or by means of its comparative density, accentuates the shadows of calculi in the urinary tract when they are not ordinarily seen in the plain roentgenogram.

NOTES ON NEW BOOKS.

Diseases of the Eye. By GEORGE E. DE SCHWEINITZ. Eighth edition. Cloth, \$6.00. (Philadelphia: W. B. Saunders Company, 1916.)

It is a common weakness in the writings of men who have had their training along ultra-pathological lines that the element of practical application is obscured by the ætiological, histological and allied considerations. Fuchs' inestimable text-book has been rendered as practical as it is because of Alexander Duane's parenthetically inserted notes.

Similarly, in the earlier editions of de Schweinitz' book, the minutiae of the therapeutic sections were lacking, and the practitioner, seeking to apply the outlined treatment to a given case, could not always find, in the text, the proportions of the suggested remedies.

Furthermore, the section on extraocular muscles and the orthoptic, gymnastic procedures variously employed for derangements in them were also slighted in the earlier volume. On these grounds one ophthalmologist, having felt this to be a great drawback, has criticised de Schweinitz' work somewhat severely.

The more recent editions have been gradually perfected, and we have, in the last revision, a work truly comparable with Fuchs' production, and, certainly, the leading ophthalmological text-book in the English language.

With the incalculable advantage of an early start in his writings de Schweinitz has been able to review his own work repeatedly, while still in the heyday of his active career; and because of these revisions the book is thoroughly up to date in every particular and is one which can, with safety and profit, be used as a guide by the practitioner.

The most important addition to this eighth volume is the perimetric work of Clifford Walker, whose visual field studies are now classic. The consideration given these investigations proves that the broadest and most important line of oculistic endeavor, at the present time, is perimetry which, with ophthalmoscopy, as now being worked out, is recognized as the greatest and surest connecting link between ophthalmology and its parental subjects—medicine and surgery.

The section on operations is most complete. If any ophthalmic volume is ever to become as standard as Fuchs' text-book, this of de Schweinitz will be the one.

L. W.

The Principles of Diagnosis and Treatment in Heart Affections. By SIR JAMES MACKENZIE, M.D. Cloth, \$2.50. (London, Oxford University Press: Henry Froude and Hodder & Stoughton, 1916.)

Based upon the conspicuous ability for observation and careful study which has been emphasized by the surmounting of unusual obstacles to research, an almost holy reverence has grown up for the work of Sir James Mackenzie. It is, then, a little disappointing that he should have thrown together a few rather elementary lectures and philosophical comments on cardiac conditions and should have published them. From the great much is expected, and the title of this book had rather forecast a summary and conclusion of his life's work that would endure as his monument to future generations.

In reviewing the book, there are, in addition to the short and numerous notes from his rich experience that must be dug from the text, several points that merit careful consideration. In the first place, heart failure or myocardial insufficiency, as it is often designated, represents the inability of the heart to play its demanded part in the physical life of the individual. The particular lesion and its characteristic physical signs are only secondarily important. Again, clinical signs, unfortunately, fall down where cardiac efficiency is questioned; hence the need for more careful histories and more exact study of symptoms, which are, after all, the earliest signs of heart failure. Further, the knowledge of the wound is emphasized—the variance of its characteristics in different ages and under different conditions—and the fact that the diseased heart represents a physiological response to a pathological demand is stressed. And in diagnosis this book points out the impossibility, as a rule, of relying on any one sign to supply the sole basis for our conclusions.

From the patient's point of view, Sir James Mackenzie brings out the importance of prognosis. He speaks against the present

unfortunate relationship existing between the hospital and dispensary method of treating cardiac cases, in which the most experienced practitioner devotes his time to the clever but useless diagnosis in the ward of relatively incurable conditions, while the incipient and often more or less curable cases are left to a rushed and more inexperienced dispensary physician.

Above all, this book brings to the attention of the general practitioner the unique position he occupies in clinical research, in being able to study the course of cardiac cases, the progress and prognosis to be drawn from individual symptoms and signs, and their response to treatment.

E. W. B.

Instinct and Intelligence. By N. C. MACNAMARA, F. R. C. S. 8 vo, 216 pages. Cloth, \$2.00. (New York: Oxford University Press, 1915.)

The author endeavors "to give an outline of the evidence and the reasons upon which we rely to prove that the instinctive behavior of human beings depends on work performed by definite parts of the brain; consequently, education has not only to deal with the training of something immaterial which we call mind or consciousness, but has first and foremost to deal with the proper development of the nervous substance of that part of the brain, the orderly working of which is essential for the occurrence of instinctive and intellectual phenomena. In the majority of healthy children this purpose can be attained by means of the appropriate exercise of their eyes, ears, and other sensory organs; for, as we explain, energy derived from this source stimulates and develops the living substance of those parts of the brain directly concerned in the elaboration of an individual's instinctive and intellectual processes; we may thus hope to lay the foundation on which to build up a chaste, self-reliant character, combined with a clear and strong intellectual capacity."

In the main there is rather more effort spent on the consideration of the neural corollaries than on the concrete instincts and our means of forging them into intellectually controlled power. The discursive rather than intensive type of discussion of the above point of view brings together many interesting, though mostly elementary, facts for a beginner or for an hour of leisure.

The Principles and Practice of Perimetry. By LUTHER C. PETER, M. D., F. A. C. S. Cloth, \$2.50. (Philadelphia: Lea & Febiger, 1916.)

In this fascinating little book of two hundred pages, the author has not only compiled all that we have, or ought to have, read on the subject and added personal observations of great value, but has, in addition, breathed into the dry facts thus gleaned the warmth and enthusiasm of a man thoroughly engrossed in his subject.

Besides a most complete bibliography, introduction and appendix, we find a table of contents which is arranged in a group and sub-group system, making the book invaluable for quick reference to one familiar with the general subject and desirous of omitting unnecessary details. The text throughout is profusely illuminated with instructive diagrams and charts.

Perimetry is a most difficult subject to handle with any degree of dogmatism, because of the varied interpretations which may be put upon the same findings depending upon associated states. It is due to this, no doubt, that no English-speaking physician has ever before attempted a volume on this special branch of ophthalmology. For this reason, as the author says: "Dovetailing of the practical and the academic has been found to be the logical method of presenting the subject."

Dr. Peter makes a good point with which many observers will agree. He contends that most color-field averages given in the text-books are too high for the normal encountered in practice; the expressed desire for an iron-clad standardization of colors

must meet with uniform approval, it being well appreciated, for example, that a deep orange-red will give a larger field than a true red.

His statement, however, that in man overlapping of the visual fields reaches its highest degree, will not be accepted by some of his readers.

Another item of practical import is that the taking of fields is a matter of training to the most literate patient, the first records not being dependable and that for the sake of accuracy several remeasurements are necessary.

To oculists who deplore the careless field-taking of most surgeons, it is refreshing to see emphasis laid upon the size of the blind spot and the zone of impaired color sensation about it.

The reviewer, personally, does not agree with the author's grounds for his preference for the daylight illuminated perimeter over the electrically transilluminated instrument, because the former varies with bright or cloudy days, and the time of the day, as well as the direction of the light, whereas the latter, used in a dark room, is standard and invariable. As to the advantages of the campimeter over other scotometric devices, we are fully in accord with the author's views.

The classification of scotomata is excellent, and could profitably be accepted as standard. It is interesting to note that Peter disputes van der Hoeve's "ring of indistinct scotoma" surrounding the normal blind spot, and contends that its presence is the first sign of enlargement of the latter.

The value, in diagnosis and prognosis, of perimetry, frequently practised during the course of regressive processes in intraocular disorders, is clearly demonstrated.

The whole perimetric subject is brought under two heads: (a) General pathology of the visual fields. (b) Special pathology of the visual fields. Details are given and the visual tract is divided into groups for systematic study and isolation.

The reader is astonished at the very evident thoroughness with which the author has examined the visual fields of cases embracing, apparently, almost every condition which would show any perimetric change whatever.

An individual point not emphasized elsewhere in literature, so far as the reviewer is aware, is the presence of an indistinct, scotomatous area in the prescotomatous stage, or immediately surrounding a definite scotoma—a region in which color and form are determined, but with great uncertainty.

One of the most striking sections of the book is the one containing the assertion that reversal of the color fields in choked disk is psychic in origin, and not organic, and pointing out the fact that neoplasms in various parts of the brain may produce such a reversal.

The objection that, if Cushing's and Walker's explanation that nasal contraction of the visual fields in brain tumor with choked disk is due to pressure of the chiasm outward against the carotid arteries by the distended third ventricle is an acceptable hypothesis, there should be altitudinal changes as well, because the same force would crowd the chiasm down upon its bony bed in the sphenoid, is well taken. Peter's explanation of the phenomenon on other grounds is well worth consideration. He says that, because of the eccentric location of the disk, and the fact that "the temporal distribution of the optic nerve is accomplished by a longer and more circuitous route than the direct radiations of the nasal retina," he regards the nasal contraction as a purely intraocular affair such as occurs in glaucomatous atrophy. He quotes Siemerling's case for proof of the pathological contention that distention of the third ventricle would be more apt to produce bitemporal than binasal hemianopsia.

There is a splendid summing up of the various changes in glaucomatous fields with points on perimetric diagnosis.

In diseases of the optic nerve proper, the visual field changes characteristic of the various forms of posterior sinus disease are

clearly demonstrated and lucidly explained, the findings of Markbreiter and others, who have recently conducted classical investigations into this particular branch of perimetry, being carefully tabulated for the rhinologist's benefit.

In discussing toxic amblyopia, it is interesting to note that Peter gives some preference to the less popular theory that the process begins in the ganglionic cells of the retina, secondarily spreading to the nerve fibres or papillo-macular bundle and not conversely.

There is an excellent section on fields in disease of the chiasm, with the various views as to the *modus operandi*, richly illustrated with charts. Under this heading, Peter warns against the bizarre and heterogeneous fields of organic chiasmal disease frequently complicated by hysteria, with the consequent double and misleading perimetric findings.

Under diseases of the optic tracts, the author agrees with Hess and Walker that the Wernicke pupillary phenomenon and the Wilbrand prism phenomenon are of no value in localization of a lesion in, or anterior to, the basal nuclei from one above these nuclei in the optic radiations and cortex. But he believes that, if the technic is perfected to more scientific precision, the former test may be of value in locating the seat of the lesion in hemianopic central amblyopia.

The section on diseases of the optic radiations is really fascinating, and of great interest to the neurologist as well as the ophthalmologist.

The best section of the book, however, is Part IV—Fields in Functional Nervous Diseases—wherein all the latest studies are collaborated and presented in such a systematic form that it will prove invaluable as a supplement to the studies of the neurologist or internist in the difficult differential diagnoses so often confronting them.

Altogether, this little volume is one well worth having, and grows upon one with each reading.

It is to be hoped, however, now that the first edition has been received so well, that Dr. Peter will soon present the subject in still greater detail and technicality, for it is one of unending possibilities.

L. B. W.

Physical Diagnosis. By JOHN C. DA COSTA, JR., M. D. 3d edition. Cloth, \$3.50. (Philadelphia and London: W. B. Saunders Company, 1915.)

The subject matter, arranged as in preceding editions, has been somewhat enlarged. The illustrations are good and original. The topographical charts add much to the clearness of the text. The pathology of diseased conditions is briefly treated along with descriptions of the physical findings. Diagnosis by means of the electrocardiograph, the sphygmomanometer and the X-Ray is discussed and examples are given in their proper places. This should prove a very useful book.

M. A. H.

Obstetrics, Normal and Operative. By GEORGE PEASLEE SHEARS, M. D. Cloth, \$6.00. (Philadelphia: J. B. Lippincott Company, 1916.)

This recent addition to the rapidly growing number of text-books of obstetrics is an attempt, as the author says in the preface, to eliminate the irrelevant matter usually present in such works and to give more attention to the practice of obstetrics. The result is a one-man book with many glaring inaccuracies and omissions. There is throughout the work an evident lack of familiarity with the recent scientific literature. The author in large part relies upon his own personal experience, but does not substantiate his assertions with any actual figures. There are numerous unnecessary repetitions and cross-references that tend to annoy the reader and distract his attention.

As examples of the inaccuracies might be cited the reference to obstetrician as a word of Greek derivation, the statement that

the urea and ammonia determination require two or three days' work, that syphilis is the most common cause of abortion, that occiput posterior positions are usually associated with disproportion, that the blood loss in a normal labor is 80-100 gm., that rickets is hereditary and so on. In speaking of acute yellow atrophy of the liver it is stated that it occurs so frequently among pregnant women that it was called "icterus gravis" by the older writers.

Several practical points are entirely omitted: rectal examinations during labor are not mentioned, nor is tamponing the uterus after delivery in cases of placenta prævia; manual rotation of the head before applying forceps is scarcely considered. Delivery of the head by the Ritgen maneuver or some modification of it is not included in the discussion of a normal delivery. Chronic nephritis is treated separately from the other toxemias and, in spite of its frequency and the excellent results obtained by reasonably intelligent treatment, the entire discussion is contained in 22 lines and the only treatment mentioned is the termination of the pregnancy. On the other hand, asphyxia neonatorum is given 22 pages and 14 large illustrations, five of which picture the Sylvester and Schultze methods, neither of which has anything to recommend it in the treatment of this condition.

The author's chemical views are put forth in such a manner as to be very confusing. Sub-oxidation, a very indefinite term, is used to explain the manifold metabolic disturbances of pregnancy and a theory of the cause of eclampsia is based upon this unproven deprivation of the tissues of oxygen. In fact the lack of oxygen is blamed for many things and the therapeutic use of the gas is recommended in almost every condition for the mother and child. The observation upon the fetal heart rate when the mother is given oxygen by inhalation is so opposed to current physiological opinion that it needs to be confirmed by some more exact procedure before being accepted as an exception to the usual result of increasing the oxygen supply.

In general the advice given is sound and in conformity with modern conservative prevention and therapy; but occasional dangerous bits of teaching are noted. It is stated that 2½ or 3 hours' first-stage pains without progress supply an indication for forceps and the author further states that when a patient says she "can bear it no longer" she should be delivered instrumentally. It is truly pernicious to propagate such views among the physicians of the country who are already far too radical in their use of artificial methods of delivery.

The illustrations are mostly quite familiar and practically the only original ones are reproductions of photographs which, although exemplifying the photographer's art, do not rank very high in the realm of medical illustration.

E. D. P.

Diseases of the Skin. By HENRY H. HAZEN, M. D. Cloth, \$4.00. (St. Louis: C. V. Mosby Company, 1915.)

It is true, as the author states in his preface, that an apology is needed for adding another text-book on diseases of the skin to the many now available. But if an author can demonstrate good reasons for his work, such as a departure from the usual methods of treating his subject—in other words, if he shows originality or the emphasizing of important aspects—we are obligated at least to become acquainted with his presentation. Dr. Hazen, writing especially for students and practitioners, has departed from the usual text-book methods in several ways. He has given a classification of diseases for the most part based on etiologic or pathologic, rather than on anatomic, grounds; moreover he has emphasized the pathologic and histo-pathologic aspects especially of the commoner diseases—a factor which we believe to be of the highest importance for the teacher and of the greatest significance for the pupil.

We welcome particularly the chapters on etiology, symptomatology, diagnosis, treatment and hygiene as concise yet fairly com-

plete presentations of the most important aspects of study of the various dermatoses. A text-book of this size and purpose must of necessity be so brief that the author is constrained to become rather dogmatic in his statements. We must, therefore, accept with a certain amount of reserve various statements made in the section on etiology. The discussion on symptomatology is good, especially on that of occupational diseases.

The methods recommended for diagnosis are based, as the author states, on the splendid little system arranged by Dr. Gilchrist for use in his teaching in The Johns Hopkins University courses. The author uses a modification of this, which means that the disease is diagnosed by a consideration of the primary lesion, the arrangement and distribution of lesions, the objective symptoms etc., the system being used very much as a key similar to that in a text-book on botany or the like.

The chapters on therapy and hygiene are sufficiently complete for a book of this size. We are pleased to note that sufficient space is given to X-Ray therapy which has won for itself, in recent years, such an important place in the alleviation of skin disorders. A very brief account only is given of radium, and too little of electrolysis—two very important agents in the therapeutic armamentarium. The sections on hygiene and on professional and trade dermatoses are clear, brief, and very practical.

We are pleased to note many excellent prescriptions which are written in the metric as well as in the usual system; but some of these require correction and would be more instructive were they written out in full, especially for the student who is frequently not too well equipped in this important part of medical training.

There are a few points of minor importance to which attention may be directed, such as the use of the term "barber's itch" as a synonym for two different diseases; namely, sycosis vulgaris and sycosis parasitica. In the section on tuberculosis of the skin (lupus vulgaris) the author makes no mention of the importance of a generalized or a pulmonary tuberculosis as a probable accompaniment of the disease of the skin.

In a brief review such as this it would be difficult to discuss every section; but attention should be called especially to the excellent sections on eczema and on syphilis.

It is unfortunate that nearly every photomicrograph is practically worthless because the histologic changes are so poorly depicted. But too much praise cannot be given for the excellent photographs, most of which we know, from personal association, have been made by the author and his teacher and associate, Dr. Gilchrist. A good photographic representation of a disease of the skin is the most eloquent kind of description and the most lasting for the student mind.

Like many books of its kind it is up to date, especially in the adequate summaries of many of the rare diseases. It has the advantage that the author always gives an account of his own experiences and work in dermatologic fields—which, if not always in accord with the usual opinions of other and older dermatologists, at least makes the book individual. In this connection, also, the book expresses, as the author states in his preface, many of the views and some of the therapeutic measures adopted by the dermatologic staff of The Johns Hopkins Hospital. Furthermore, the author has taken pains to give his findings in studies of skin diseases in the negro, which are always instructive and interesting, at least by way of comparison.

The book is attractively bound, is very handy, and when proper correction is made of the occasional typographical errors, it can well make a claim for use as a text-book for the student, who has not the time to read the more comprehensive works, and for the practitioner who is too busy to delve too far into the possibilities of a puzzling diagnosis.

I. R. P.

Skin Cancer. By HENRY H. HAZEN, M. D. Cloth, \$3.00. (St. Louis: C. V. Mosby Company, 1916.)

This is a book primarily for the clinician and deals not only with skin cancer and cancerous lesions but also with skin lesions which might be mistaken for cancer. The description of cause and symptoms is brief but complete. The subject of differential diagnosis is well summarized in a separate chapter. In addition to this there is an excellent chapter dealing with treatment in a way which is neither too radical nor too conservative. The book is well arranged and very readable. It offers an excellent résumé of the subject of cancer of the skin. It cannot be too highly recommended to the profession, for it is a thoroughly modern treatise.

J. C. L.

Blood-Pressure, from the Clinical Standpoint. By FRANCIS ASHLEY FAUGHT, M. D. Second edition. Cloth, \$3.25. (Philadelphia: W. B. Saunders Company, 1916.)

The practitioner will find in this book a complete and well-balanced summary of the ponderous literature of late years upon this important subject. The whole is tempered by the author's good scientific insight and conservative clinical judgment. In the preface the writer begs latitude from the strictly scientific investigator for his attempt to draw clinical conclusions from laboratory data, but one is rather struck by the absence of the attempt to elaborate his own hypotheses without a substantial background of fact.

The text is introduced by a review of the physiology of the circulation and of the factors concerned in the maintenance of blood-pressure. The various methods for estimating blood-pressure are discussed and the instruments to be used are described, under their market names, in detail. The blood-pressure in health and the effect upon it of various external factors—race, climate, altitude, age etc., are also dealt with.

Then follows the clinical application and the subject of blood-pressure is correlated with the following conditions—acute infections (with sub-headings), arteriosclerosis, nephritis, cardiac disease, surgical operations and obstetrics and in its relation to life insurance. There is an appendix upon the therapeutics of hypertension.

The book does not mark an epoch in the study of blood-pressure, but, with a few very minor exceptions, it is a careful compilation of our knowledge, to date, of this subject.

J. T. K., JR.

International Clinics. A Quarterly of Illustrated Lectures and Especially Prepared Original Articles. Vol. III. Twenty-sixth series. Cloth. (Philadelphia and London: J. B. Lippincott Company, 1916.)

Any comment upon this work would be entirely superfluous. The name is all that is necessary to recommend the perusal of its contents. Of especial importance in this volume is the consideration of pneumothorax and tuberculosis, both from a clinical and roentgenological standpoint.

Urgent Surgery. By FELIX LÉJARS, translated from the seventh French edition by WM. S. DICKIE, F. R. C. S. Vol. 1. Cloth, \$7.00. (New York: William Wood & Co., 1914.)

This book offers very little to recommend itself under such a title. It is extremely redundant, both in writing and illustrations. It is written in the first person and the present tense and becomes tiresome reading. The subjects are handled in a scattered, diffuse manner and one gains a very poor impression of what one should do in cases of urgent surgery. In short, there is nothing in this book, that is not found in any of the minor text-books of surgery, where the subject will be found presented in a very much more logical and succinct manner.

Cerebellar Abscess, Its Etiology, Pathology, Diagnosis and Treatment. By ISIDORE FRIESNER, M. D., and ALFRED BRAUN, M. D., F. A. C. S. Cloth, \$2.50. (New York: Paul B. Hoeber, 1916.)

This is a very comprehensive and excellent treatise on abscess of the cerebellum. As an introduction, there is a very good consideration of the anatomy and physiology of the cerebellum. The etiology, pathology, symptoms, prognosis and treatment are separately and quite thoroughly considered. There is a very good bibliography.

Practical Bandaging, Including Adhesive and Plaster-of-Paris Dressings. By ELDRIDGE L. ELLISON, A. B., M. D. Cloth, \$1.50. (Philadelphia and London: J. B. Lippincott Company, 1914.)

This is a small book giving illustrations of the bandages most commonly used. There is nothing especially new, the bandages being mostly of the type found in all text-books. Many of the newer bandages that possess more or less individuality are not included. The book, however, is very well condensed and should be useful for the medical student.

Studies in Surgical Pathological Physiology from the Laboratory of Surgical Research. New York University. Vol. I. Cloth. (New York University, 1915.)

The value of this work lies in the stimulus for experimental observation in surgical laboratories. It includes quite a fund of experimental work bearing upon practical problems. The papers are presented in their original form, as the subjects are so diffuse as not to allow their arrangement in any systematic grouping. The caliber of the articles necessarily varies, but most of them will be found valuable by those engaged in experimental work.

Bone Graft Surgery. By FRED H. ALBEE, A. B., M. D., F. A. C. S. Cloth, \$6.00. (Philadelphia and London: W. B. Saunders Company, 1915.)

Because of the importance of Albee's contributions to bone surgery, notably transplantation for tuberculosis of the spine and inlay graft, both of which he has done so much to develop, this book has been looked forward to with considerable interest. These two subjects have received the brunt of the author's attention in this volume, both being very well presented and profusely illustrated. His own technique, which is so efficiently developed, is very clearly demonstrated and should be very helpful to those interested in bone surgery.

The treatment of fractures of the femur and fractures of the os calcis and patella with bone pegs is also a very distinct advance, and shows the development of the author's technique. The entire book is most valuable for those interested in bone surgery.

Localization by X-Rays and Stereoscopy. By SIR JAMES MACKENZIE DAVIDSON. Cloth, \$3.00. (New York: Paul B. Hoeber, 1916.)

The author discusses the various methods employed in locating various bodies. He does not confine himself to the roentgenological methods, but includes others, for instance, those in which the telephone and electro-magnet are used.

The methods described, although somewhat complicated, are very exact and should be of great assistance, particularly in locating deep-seated bodies.

The chapter dealing with the exact localization of deep-seated bodies in the eye is most interesting and instructive. The technique is very accurate and consequently the results are uniformly good.

Throughout the book various ingenious techniques are given, which the author employs not only in the subject under discussion but also in his general roentgenological work.

The final chapter discusses protection for the roentgenologist. This is particularly opportune, since the great amount of localiza-

tion that is being done incidental to the war is beginning to show some harmful effects upon the roentgenologists.

This book should be very valuable to all roentgenologists, but particularly to those who are operating in large industrial centers where the need of localization of foreign bodies is very great.

F. H. B.

Diagnosis and Treatment of Surgical Diseases of the Spinal Cord and Its Membranes. By CHARLES A. ELSBERG, M. D., F. A. C. S. Cloth, \$5.00. (Philadelphia and London: W. B. Saunders Company, 1916.)

Treatises on surgery of the spinal cord are quite infrequent and for this reason this book is received with considerable interest and should be of much assistance. It is mainly a summary of the author's experiences. The technique of his operations and the general run of cases that he has encountered give one a very good idea of surgery and surgical conditions of the spinal cord. The part on tumors of the spinal cord is particularly good, especially from a pathological and operative standpoint. The subjects are well presented, although somewhat redundant. The illustrations are good.

A Text-Book of Physiology for Medical Students and Physicians. By WILLIAM H. HOWELL, PH. D., M. D., Sc. D., LL. D., Baltimore, Md. Sixth edition, thoroughly revised. Cloth, \$4.00 net. (Philadelphia and London: W. B. Saunders Company, 1915.)

The sixth edition of any text-book calls for but brief consideration in this place because its field of usefulness has been established. Howell's Physiology has maintained its preeminence for two chief reasons: First, because the author has retained a thoroughly modern point of view in dealing with the various phases of a now complex subject, as is indicated by his treatment of the newer literature; and second, because the style of presentation is simple and clear. An illustrated text-book of physiology which accomplishes these ends, and yet is held within a thousand octavo pages of ten-point type, is worthy of its success.

The Origin and Nature of the Emotions. By GEORGE W. CRILE, M. D. Cloth, \$3.00. (Philadelphia and London: W. B. Saunders Company, 1915.)

In this volume eight addresses delivered by Dr. Crile before various societies during the past few years have been brought together. The titles of the addresses give a clue to their contents and are as follows: (1) Phylogenetic Association in Relation to Certain Medical Problems; (2) Phylogenetic Association in Relation to the Emotions; (3) Pain, Laughter and Crying; (4) The Relation Between the Physical State of the Brain-Cells and Brain Functions—Experimental and Clinical; (5) A Mechanistic View of Psychology; (6) A Mechanistic Theory of Disease; (7) The Kinetic System; (8) Alkaescence, Acidity, Anesthesia—a Theory of Anesthesia.

The author of these addresses has a fertile imagination and delights in attempting the formulation of general laws that epitomize the data slowly accumulated by clinical and pathological research. In the papers before us he attempts to correlate many of the known facts of surgical pathology and physiology with facts of general biology. Thus after discussing the phylogenetic origin of the emotions, for example, he tries to establish the pathological identity of surgical and emotional shocks. With the aid of laboratory associates, he supports his views based upon clinical observations with laboratory studies (histological, chemical, physiological).

In the experimental work, animals were subjected to fear and anger, to infection and to protein poisoning, and later the histological changes in the organs and tissues were studied. Crile describes certain alterations in the brain, the adrenals and the liver, that he believes are due to emotion, infection, or poisoning. Since the changes were limited to the three organs mentioned,

he groups these organs together into what he calls the "kinetic system" and suggests that no member of the system can act without the cooperation of the other two. The changes that the organs of the kinetic system undergo in the ordinary wear and tear of life are repaired largely, he believes, during sleep, a view which he also supports by experiments on animals.

Crile, in a pleasing way, draws upon the researches and hypotheses of Darwin, of Sherrington, and of Cannon, to interpret his

clinical studies and his experimental observations. The book makes interesting reading and though conservative workers will probably withhold judgment regarding the interpretation of the histological findings and of the experiments pending further studies, still the book should be stimulating to thought and research and will be read by physicians, medical students and biologists with interest and pleasure. The illustrations add to the attractiveness of the several papers. L. F. B.

BOOKS RECEIVED.

Bacteriology, General, Pathological and Intestinal. By Arthur Isaac Kendall, B. S., Ph. D., Dr. P. H. Illustrated with 98 engravings and 9 plates. 1916. 8°. 651 pages. Lea & Febiger, Philadelphia and New York.

Stanford University Medical Publications. Bulletin No. 3, 1914-1915. 1915. 4°. San Francisco.

American Ophthalmological Society. Transactions of the American Ophthalmological Society. Fifty-second Annual Meeting, Washington, D. C. Vol. XIV, Part II. 1916. 8°. Philadelphia.

Carnegie Endowment for International Peace. Founded December 14, 1910. Year Book for 1916. 8°. 204 pages. Washington, D. C.

A Practical Treatise on Disorders of the Sexual Function in the Male and Female. By Max Hühner, M. D. 1916. 8°. 318 pages. F. A. Davis Company, Philadelphia; Stanley Phillips, London.

The Backwash of War: The Human Wreckage of the Battlefield as Witnessed by an American Hospital Nurse. By Ellen N. La Motte. 1916. 16°. 186 pages. G. P. Putnam's Sons, New York and London.

Syphilis and the Nervous System. For Practitioners, Neurologists and Syphilologists. By Dr. Max Nonne. Authorized translation from the second revised and enlarged German edition. By Charles R. Ball, B. A., M. D. 98 illustrations in text. Second American edition, revised. 1916. 8°. 450 pages. J. B. Lippincott Company, Philadelphia and London.

Diseases of Children. By Edwin E. Graham, A. B., M. D. Illustrated with 89 engravings and 4 plates. 1916. 8°. 902 pages. Lea & Febiger, Philadelphia and New York.

The Healthy Girl. By Mrs. Joseph Cuning, M. B. (Lond.), and A. Campbell, B. A. 1916. 12°. 191 pages. Henry Froude, London; Hodder & Stoughton, London.

A Purin-Free Dietary: Sample Menus and Recipes. By Edna Alice Waite and Robert Ellsworth Peck, M. D. 1916. 16°. 24 pages. The Peck Sanatorium, Woodmont, Conn.

Principles of Diagnosis and Treatment in Heart Affections. By Sir James Mackenzie, M. D., F. R. S., F. R. C. P., LL. D. Ab. and ed., F. R. C. P. I. (Hon.). 1916. 8°. 264 pages. Henry Froude, London; Hodder & Stoughton, London.

The Control of Hunger in Health and Disease. By Anton Julius Carlson. 1916. 8°. 319 pages. The University of Chicago Press, Chicago, Illinois.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by H. R. M. Landis, M. D. Twenty-sixth series. Volume III. 1916. 8°. 307 pages. J. B. Lippincott Company, Philadelphia and London.

Infections of the Hand. A Guide to the Surgical Treatment of Acute Chronic Suppurative Processes in the Fingers, Hand and Forearm. By Allen B. Kanavel, M. D. Third edition, thoroughly revised. Illustrated with 161 engravings. 1916. 8°. 499 pages. Lea & Febiger, Philadelphia and New York.

Cornell University Medical Bulletin. Volume VI. Number 1. July, 1916. Studies from the Department of Roentgenology. Published by Cornell University, New York City.

A Manual of Otology. For Students and Practitioners. By Charles Edwin Perkins, M. D., F. A. C. S. Illustrated with 120 engravings. 1916. 12°. 445 pages. Lea & Febiger, Philadelphia and New York.

The Diagnosis and Treatment of Digestive Diseases. A Practical Treatise for Students and Practitioners of Medicine. By George M. Niles, M. D. With one colored plate and 86 other illustrations. 1914. 8°. 597 pages. P. Blakiston's Son & Co., Philadelphia.

Diseases of Occupation and Vocational Hygiene. Edited by George M. Kober, M. D., LL. D., and William C. Hanson, M. D. With illustrations and reference tables. 1916. 8°. 918 pages. P. Blakiston's Son & Co., Philadelphia.

Collected Reprints. By Theodore Caldwell Janeway, M. D. 1901-1914. 4°. Baltimore.

The Clinics of John B. Murphy, M. D., and Mercy Hospital, Chicago. Edited by P. G. Skillern, Jr., M. D., of Philadelphia. Vol. V, No. 4, August, 1916. 1916. 8°. W. B. Saunders Company, Philadelphia and London.

Studies from The Rockefeller Institute for Medical Research. Reprints. Vol. XXIV. 1916. 8°. 515 pages. The Rockefeller Institute for Medical Research, New York.

The Institutional Care of the Insane in the United States and Canada. By Henry M. Hurd, William F. Drewry, Richard Dewey, Charles W. Pilgrim, G. Alder Blumer and T. J. W. Burgess. Edited by Henry M. Hurd, M. D., LL. D. Vol. II. Illustrated. 1916. 8°. 897 pages. The Johns Hopkins Press, Baltimore.

Hospital of the Protestant Episcopal Church in Philadelphia. Medical and Surgical Reports of the Episcopal Hospital. Volume III. 1915. 8°. 356 pages. Press of Wm. J. Dornan, Philadelphia.

American Year-Book of Anesthesia and Analgesia. By F. H. McMechan, A. M., M. D., editor. 1915. 4°. 416 pages. Surgery Publishing Company, New York City.

Medical Society of London. Transactions of the Medical Society of London. Volume XXXIX. 1916. 8°. 332 pages. Harrison & Sons, London.

Home Care of Consumptives. By Roy L. French, M. A. With 27 illustrations. 1916. 12°. 224 pages. G. P. Putnam's Sons, New York and London.

Care and Feeding of Infants and Children. A Text-Book for Trained Nurses. By Walter Reeve Ramsey, M. D. Including Suggestions on Nursing, by Margaret B. Lettice and Nann Gossman. 123 illustrations. Lippincott's Nursing Manuals. [1916.] 8°. 290 pages. J. B. Lippincott Company, Philadelphia and London.

University of Iowa Monographs. Studies in Medicine. Volume I. Number 1. June, 1916. Collected Studies and Reports. Published by the University.

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THE D:N RATIO IN DIABETES MELLITUS.

By HERMAN O. MOSENTHAL AND D. SCLATER LEWIS.
(From the Medical Clinic of The Johns Hopkins Hospital.)

Minkowski,¹ observing depancreatized dogs, was the first to recognize the importance of the proportion of urinary glucose, not derived from carbohydrate of the food, to the urinary nitrogen. When the diabetic organism does not utilize ingested carbohydrate, this appears in the urine. As the disease progresses, the carbohydrate derived from protein likewise is not utilized, and appears in the urine. There is at present no convincing evidence that fat may give rise to glucose.² The amount of protein metabolized may be estimated from the quantity of urinary nitrogen. The ratio of unutilized glucose which is derived from protein to the urinary nitrogen, the dextrose-nitrogen, or, in short, the D:N ratio, may, therefore, be regarded as a measure of the intensity of the diabetes.

¹ Minkowski: Arch. f. exp. Path. u. Pharm., 1893, XXXI, 85.
² Allen, F. M., and Du Bois, E. F.: The Archives Int. Med., 1916, XVII, 1010.

1. THE MAXIMAL D:N RATIO.

Lusk³ and his collaborators have investigated the D:N ratio of phlorhizin diabetes. They have definitely established the maximal ratio at 3.65:1, which signifies that 58.4 per cent of protein and no more is available to the organism as glucose. Very few human cases of diabetes mellitus have been observed to exhibit this maximal ratio.⁴ The obstacles attending such

³ Lusk, G.: Ergebn. d. Physiol., 1912, XII, 315.
⁴ Mandel, A. R., and Lusk, G.: Deutsch. Arch. f. klin. Med., 1904, LXXI, 472.
Lusk, G.: The Arch. Int. Med., 1912, X, 122.
Foster, N. B.: Deutsch. Arch. f. klin. Med., 1913, CX, 501.
Greenwald, I.: Jour. Biol. Chem., 1914, XVI, 375; Jour. Biol. Chem., 1914, XVIII, 115.
Allen, F. M., and Du Bois, E. F.: The Arch. Int. Med., 1916, XVII, 1010.
See also Lusk, G.: The Arch. Int. Med., 1909, III, 5.

studies will be discussed in the second part of this article. Under these circumstances, even a single case is worth a great deal in establishing the true maximal ratio for human diabetes. For this reason the following record is of interest:

E. W. (Medical No. 35092), female, married, white, aged 51, was admitted to the medical clinic of The Johns Hopkins Hospital November 28, 1915. The history as obtained at the time of and previous to her fatal illness differed somewhat, as might be expected in an irresponsible individual. The main facts, however, were these:

Family and Past History are unimportant except for the fact that nearly every member of the family has been obese.

Present Illness: In 1899 there was thirst, loss of weight and pruritus vulvæ. Three months later, glucose was demonstrated in the urine. The symptoms cleared up rapidly with a reduction of the starchy food. She soon began to break diet; glycosuria has been present almost constantly since that time. There have been four admissions to the hospital, the last one 6 months ago, during each of which she was made sugar-free, though with increasing difficulty. Attendance at the diabetic class of the dispensary was very irregular and without therapeutic result. There has been marked loss of weight and strength. In 1899, the patient weighed about 180 pounds, although only 5 feet 4 inches in height. The present weight is 123 pounds. Four years ago she was treated in this hospital for carcinoma of the cervix; 3 years ago the growth was removed by means of the actual cautery and subsequent radium treatment was resorted to. For five years there have been sharp pains in the arms and legs, which improved on the rare occasions when an antidiabetic diet was adhered to. Three years ago, pains in the right upper quadrant of the abdomen were diagnosed as due to a movable kidney kinking its ureter. No operation was performed because of the diabetes. During this period of 5 years of suffering, the patient has had recourse to morphine, using from one-half to three grains a day. Two weeks before admission to the hospital, a bunion on the left foot became red, swollen and tender. This swelling has gradually been in-

creasing. For the past two days there have been drowsiness and shortness of breath.

Physical Examination on Admission: T. 102.6°. P. 112. R. 26. Weight 123 pounds. Height 5 feet 4 inches. The patient is drowsy; there is a moderate degree of air hunger; the skin is dry and rough; there are numerous hypodermic scars; the skin is wrinkled, indicating the loss of much weight. The pupils are unequal; the right reacts sluggishly to light, the left is inactive. In the eye-grounds there are large patches of what appear to be exudate, most marked about the macula; a few hemorrhages are scattered over the retina. The thyroid gland is large and of elastic consistency, without a bruit or other sign of increased vascularity. The lungs are negative except for signs of a moderate grade of emphysema. The heart is negative. The liver edge is three finger-breadths below the costal margin. The spleen is not felt. In the right flank, a rather irregular mass, presumably an enlarged right kidney about 15 cm. in diameter, is felt. The left kidney is readily palpated. The knee-jerks cannot be obtained. On the dorsum of the left foot there is a sinus leading to an infected bunion; dead bone is felt on probing. The systolic blood pressure is 170, the diastolic 80. The Wassermann reaction is negative. Hemoglobin (Sahli) 77%; white blood cells, 9880; red blood cells, 4,248,000; the phenolsulphonephthalein excretion is 42% in two hours.

Course in the Hospital. The patient was starved for five days and then given very small quantities of food for the ensuing week. Her mental condition showed marked improvement, the air hunger diminished; but on the fourth day air hunger again manifested itself and continued until death. The urine at no time became sugar-free. The infected bunion showed no tendency to heal and definite gangrenous areas appeared on the sole of the foot. The patient died suddenly while sitting up and eating on December 11th. For details of the diet, administration of bicarbonate of soda, and laboratory findings, see Table I.

Autopsy No. 4530 (Dr. M. T. Burrows).
Anatomical Diagnosis: Primary: Atrophy of pancreas, with diffuse lipomatosis; hyaline islands of Langerhans. Perforating

TABLE I.
CLINICAL AND EXPERIMENTAL DATA OF E. W.

Date, 1915.....	November.			December.									
	28 *	29 *	30 *	1 *	2 *	3	4	5	6	7	8	9	10
Urine Vol. c. c.....	3015	3550	3500	3925	3725	3340	3600	3900	4470	4710	5940	5620
Urine Sp. G.....	1021	1020	1017	1017	1015	1015	1014	1015	1015	1014	1012	1011	1012
Urine Reaction.....	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.	ac.
Urine acidosis as B-oxybutyric ac., gm....	40.0	61.5	54.2	64.9	66.0	50.6	64.9	78.0	111.2	106.6	73.0	85.6
Alveolar CO ₂ tension, mm. Hg.....	23.3	35.0	19.5	24.6
Urine, total N, gm.....	12.4	15.6	13.0	10.2	10.8	9.8	9.0	9.6	10.5	8.9	8.7	9.9
Urine NH ₃ , gm.....	2.9	4.7	4.2	4.3	4.5	4.2	3.9	4.4	4.4	4.0	4.2	3.8
Urine, 100 $\frac{\text{NH}_3-\text{N}}{\text{N}}$	21.0	19.5	25.0	27.0	34.8	34.4	35.1	36.0	37.7	34.8	37.0	40.2	31.8
NaHCO ₃ , gm. by mouth.....	72	72	84	60	32	32	48	40	38
NaHCO ₃ , gm. by infusion.....	14	31	32	36	40	36
Blood sugar, %.....	.3325	.2421
Urine glucose, %.....	2.62	2.34	1.56	.70	.94	1.08	1.09	.88	.90	.85	.74	.60	.71
Urine glucose, gm.....	70.6	55.4	24.5	36.9	40.3	36.3	31.9	35.1	38.0	34.7	35.7	40.0
Carbohydrate intake, gm.....	0	0	0	0	0	2.5	6.0	2.0	3.7	3.0	3.7	14.1
Carbohydrate balance, gm.....	-70.6	-55.4	-24.5	-36.9	-40.3	-33.8	-25.9	-33.1	-34.3	-31.7	-32.0	-25.9
D : N.....	5.69	3.55	1.89	3.64	3.71	3.46	2.89	3.44	3.28	3.58	3.68	2.62
<i>Diet:</i>													
Total calories.....	405	385	370	105	110	120	330	305	500	585	445	220
Whiskey, c. c.....	100	80	90	40	24	8
Wine, c. c.....	360	490	345	60
Broth, c. c.....	500	500	400	400	400	400	500	500	500	500	500	300
Green vegetables, gm.....	6	85	125	78	100	55	90
Oatmeal (dry), gm.....	20
Eggs, number.....	1	1	1	1	$\frac{1}{2}$

* On these days the 24-hour collection of urine was incomplete. 500 to 1000 c. c. were lost. The volume of urine, as indicated in the table, includes the probable quantity lost. On subsequent days, not marked with an asterisk, the patient was in charge of a special nurse and the collections of urine were satisfactory.

ulcer of left foot. *Subsidiary:* Occlusion of intravesical portion of right ureter; hydronephrosis (right). Hypertrophy of left kidney. Chronic cholecystitis. Localized fibrous peritonitis. Myomata of uterus. Old operation: amputation of cervix. Pulmonary emphysema. Colloid goitre. Arteriosclerosis.

The body is that of a fairly nourished white woman. There is a considerable amount of subcutaneous fat. There is a large bunion at the distal end of the first metatarsal bone of the left foot. Between the first and second metatarsal bones there is a small perforating gangrenous ulcer. The tendon sheaths and the subcutaneous tissue of the foot bounding this ulcer are infiltrated with thick, grayish-yellow pus. The arteries are open to the edge of the ulcer where they are obliterated. The wall of the ulcer is ragged but not indurated.

The liver weighs 1700 gm. The surface is smooth except for a few adhesions to the great omentum along the inferior surface of the right lobe and in the neighborhood of the gall-bladder. The gall-bladder is small. Its wall is thickened and of a grayish color. It contains four small jagged stones and a small amount of yellowish-brown bile. There is no obstruction or partial occlusion of any of the bile-ducts.

The pancreas is much reduced in size, is everywhere infiltrated with fat; weighs 81 gm. The lobules which are present are firm.

The right kidney is a large fluctuating mass. It measures 14 x 13 cm., and although slightly lobulated, it is almost spherical in outline. The ureter is dilated, having a cross diameter of 0.9 cm. The dilatation is uniform and continuous to the bladder wall, where the ureter is completely obliterated. The kidney sac and ureter are filled with a clear fluid, which does not resemble urine, nor does it contain acetone.

The left kidney is greatly enlarged; it weighs 400 gm. The capsule is thin and strips easily. The hyperplasia as seen in this kidney is limited largely to the cortex. The cortex is thickened everywhere; it measures 8 to 10 mm.

MICROSCOPICAL NOTES.

Pancreas: The picture is that of a pronounced atrophy of the secreting epithelium of the gland. In isolated areas the gland appears normal, but in the greater part of the section the epithelial cells are decreased in size. Many acini have become reduced to a small clump of sharply staining nuclei, surrounded by a very small amount of a granular pink-staining cytoplasm. The atrophic changes are seen in every lobule and in some they are extreme. Whole lobules have become reduced to small contracted masses of connective tissue in which only the ducts can be identified. The same changes are seen in sections from the head, body and tail of the pancreas. In none is there any evidence of an increase of fibrous tissue, but rather a shrinking together of the original fibrous tissue. The increase of fat, noted on inspection, is only an apparent increase following an extensive atrophic change. The islands of Langerhans show no atrophy but an extensive hyaline degeneration. The cytoplasm of the cells stains pink and is visibly granular. The nuclei are absent in many cells, and when present are shrunken and vesicular and irregular. The nuclei of the endothelial lining of the blood sinuses are intact. In the great majority, however, the cells have become completely and uniformly hyaline. The stain is a distinct pink color. The endothelial cells of the sinuses are swollen and stand out prominently; many have degenerated into the lumen of the sinuses. The nuclei of many are pycnotic and in some cases shrunken and vesicular in shape. A few of the islands are breaking down; along the sinus walls there are vesicles in which are many pycnotic nuclei, surrounded by a small amount of cytoplasm.

Throughout these studies, the nitrogen was determined by the Kjeldahl method, the urinary ammonia by Steel's modification of

Folin's method,⁵ the urinary glucose by Benedict's modification of Fehling's solution,⁶ the acetone substances in the urine by Shaffer's⁷ procedure, the blood sugar by the method of Lewis and Benedict,⁸ the tension of carbon dioxide in the alveolar air, in samples collected by the Plesch method as modified by Higgins,⁹ by Haldane's¹⁰ method for gas analysis; and the food values were calculated from the tables of Atwater and Bryant,¹¹ with a few exceptions in which we made our own analyses.

All the data in the case of E. W. point to the fact that this patient is suffering with a diabetes of maximal severity. The height of the D:N ratio indicates that no glucose from either carbohydrate or protein is being utilized. The large quantities of acid substances excreted in the urine surpass in amount, at least during the last few days of the illness, the maximal yield of about 35 per cent¹² which can be obtained from protein. Hence, some of the β -oxybutyric acid must have its origin from both fats and proteins. It is evident that in this instance the calories ordinarily derived from starch and protein are entirely lost, those from the fats are partially made use of, and only those from the alcohol are completely metabolized. Under such circumstances, it is probable that death resulted from starvation, not because of inadequate nourishment (there was a considerable amount of subcutaneous fat), but because of inability to utilize the food offered to the tissues.

The fasting treatment of Allen did not prove itself efficient in this instance. This may be explained on the double ground of the infected bunion and of the maximal diabetes. Joslin¹³ noted that intercurrent infections frequently frustrated the efficacy of the fasting treatment. Allen and Du Bois¹⁴ find that the few known cases which have exhibited the maximal D:N ratio during fasting have died, except the patient of Geyelin and Du Bois.¹⁵

The D:N ratios in the present case were so close to the ideal maximal ratio of 3.65:1, in eight of the 12 days observed, as to be considered identical with it. The high ratio on the first day is readily explained by the fact that carbohydrate, which had been previously stored during a period of lax diet, was eliminated. The low ratio on the last day is a typical result of feeding carbohydrate—oatmeal in this instance. Such a lowering of the ratio under similar circumstances has frequently been noted and up to the present time has not been

⁵ Steel, M.: Jour. Biol. Chem., 1910, VIII, 365.

⁶ Benedict, S. R.: Jour. Am. Med. Assn., 1911, LVII, 1193.

⁷ Shaffer, P. A.: Jour. Biol. Chem., 1908, V, 211.

⁸ Lewis, R. C. and Benedict, S. R.: Jour. Biol. Chem., 1915, XX, 61.

⁹ Higgins, H. L.: Publication No. 203, Carnegie Institution of Washington, 1915, p. 168.

¹⁰ Haldane, J. S.: Methods of Air Analysis, London; Chas. Griffin & Co., Ltd., 1912.

¹¹ Atwater and Bryant: U. S. Dept. of Agriculture, Bull. No. 28, 1906.

¹² Magnus-Levy, A.: Ergebn. d. inn. Med. u. Kinderh., 1908, I, 352.

¹³ Joslin, E. P.: "The Treatment of Diabetes Mellitus," Philadelphia and New York, 1916, p. 267.

¹⁴ Allen, F. M., and Du Bois, E. F.: The Archives Int. Med., 1916, XVII, 1010.

¹⁵ Geyelin, H. R., and Du Bois, E. F.: Jour. Am. Med. Assn., 1916, LXVI, 1532.

satisfactorily explained. The ratios of 1.89:1 and 2.89:1 on the third and seventh days respectively are considerably lower than the theoretical maximal ratio. A discussion of the possible factors concerned will be taken up in the second part of this article. However, these partial exceptions do not invalidate the conclusion that the D:N ratios in this patient approximate the maximal ratio of Lusk—3.65:1—as closely as it is possible for a clinical observation to approach the fully controlled laboratory experiment. The contention that 58.4 per cent of protein and no fat is available to the human body as glucose is substantiated.

2. THE FACTORS ON WHICH THE D: N RATIO DEPENDS.

Very many reasons have been brought forward to explain the very variable D:N ratios in some cases of human diabetes. The most important of these have been the possibility of previous or present storage of sugar or glycogen, the fact that the nitrogenous and the non-nitrogenous portions of the protein molecule are not excreted with equal rapidity in the urine, the tendency of ingested carbohydrate, as in the oatmeal cure, to lower the ratio, and in instances of lax diet to raise it. These subjects are ably discussed by Joslin,¹⁶ and Benedict and Joslin¹⁷ in monographs in which they point out the impossibility of obtaining reliable D:N ratios in most cases. To sum up the situation, there is not much to be added to the statement of Rumpf,¹⁸ made some years ago, that "The intensity of the glycosuria is entirely independent and is uninfluenced by any known causes."

The essential difference between phlorhizin diabetes, in which constant D:N ratios are readily obtained, and human diabetes, in which they are not, is that the glycosuria in the former depends upon an increased permeability of the kidney to glucose, whereas in the latter, a metabolic disturbance, an inability to utilize glucose, is at fault. The relation of the permeability of the kidney to the glucose of the blood in diabetes is a question which has received but scant attention thus far. However, even the few facts gleaned at the present time indicate that this relationship is not a fixed one and consequently may result in varying levels of the D:N ratio.

In some cases of diabetes sugar does not appear in the urine, though the level of glucose in the blood surpasses the normal renal threshold of about .17%.¹⁹ This is well illustrated in Table II. Such a state is not necessarily confined to nephritis, as is often assumed, but may be brought about by other factors concerning which little is known. Martin and Mason²⁰ have recently reported similar findings. In fact, one case (Table IV), to be detailed further on, shows how nephritis is not necessarily associated with a diminished permeability of the kidney to glucose, but may even exhibit a lowered renal threshold.

¹⁶ Joslin, E. P.: The Archives Int. Med., 1915, XVI, 693.
¹⁷ Benedict, F. G., and Joslin, E. P.: Carnegie Institute of Washington, Publication No. 136, 1910, pp. 197-201.
¹⁸ Rumpf, T.: Ztschr. f. klin. Med., 1902, XLV, 260.
¹⁹ Hamman, L., and Hirschmann, I.: To be published.
²⁰ Martin, C. F., and Mason, E. H.: Am. Jour. Med. Sc., 1917, CLIII, 50.

TABLE II.
GLYCEMIA PERCENTAGE IN DIABETICS, SHOWING A BLOOD SUGAR OF .20% OR HIGHER, WHILE THE URINE WAS FREE FROM SUGAR.

Case 1.....	.20				*Case 9.....	.22			
Case 2.....	.20	.20			Case 10.....	.24	.22		
Case 3.....	.20				Case 11.....	.25	.21		
*Case 4.....	.20				*Case 12.....	.25			
Case 5.....	.20				Case 13.....	.27			
Case 6.....	.21	.20	.20		Case 14.....	.28	.20		
Case 7.....	.21				*Case 15.....	.31	.27	.25	
*Case 8.....	.21				Case 16.....	.32	.30	.21	.20

* These gave clinical evidences of nephritis; the remainder did not.

Such a raised renal threshold to glucose need not be permanent, as may be seen from Table III, which shows data from a case in which the urine contained no glucose, while the blood sugar was as high as .237%, whereas some time later sugar was excreted with a glycemia of .180% or less.

TABLE III.
DATA DEMONSTRATING THE VARIABILITY OF THE RENAL THRESHOLD TO GLUCOSE IN A CASE OF DIABETES MELLITUS.

Time.	Blood sugar.	Urine.		
			Glucose.	
	%	c. c.	%	gm.
Nov. 11.....	.237	24-hour specimen.	0	0
12.....	.220	24-hour specimen.	0	0
13.....	.180	24-hour specimen.	0	0
Dec. 1				
11.00 a. m.....	.177			
12.19 p. m.....	.180			
10.45 a. m. to 12.27 p. m.....		70	.36	.25
3.35 p. m.....	.161			
4.46 p. m.....	.181			
3.36 p. m. to 4.48 p. m.....		96	.40	.38
Dec. 8				
9.30 a. m.....	.173			
10.25 a. m.....	.142			
9.33 a. m. to 10.27 a. m.....			+	+
11.30 a. m.....	.180			
10.27 a. m. to 11.32 a. m.....			+	+

Finally, to complete the list of possible variations, the data from a case showing a distinctly lowered renal threshold may be cited (Table IV). This patient resembled in many respects the one with renal glycosuria recently reported.²¹ However, one very essential difference is apparent. The present study reveals a blood-sugar curve after the administration of 109 gm. of glucose which is characteristic of diabetes mellitus, or possibly of nephritis,²² but not of a normal person. The blood sugar rises as high as 0.26 per cent (normal 0.15 per cent); it attains its maximum only at the end of one hour (normal 15 to 30 minutes), and does not return to the fasting level for three hours (normal two hours).

The more important clinical data in this patient are:

S. B., medical history No. 36823, white, age 63. He had been treated in the out-patient department for some time, the diagnosis being chronic nephritis and hypertension; the fourth urinary examination revealed the presence of a small amount of glucose.

²¹ Lewis, D. S., and Mosenthal, H. O.: Johns Hopkins Hosp. Bull., 1916, XXVII, 133.
²² Hamman, L. F., and Hirschmann, I.: To be published.

Fehling's reaction and the fermentation test were both distinctly positive; the blood sugar at the time this specimen was passed was only 0.11%. He was admitted to the hospital for investigation; a partial result of the studies is given in Table IV. It was demonstrated that a renal glycosuria was present, and at the same time the blood sugar reaction, after the ingestion of 100 gm. of glucose, indicated a metabolism characteristic either of nephritis or diabetes mellitus; there was abundant evidence of the presence of a nephritis, with a considerable degree of diminished renal function; the urine contained a trace of albumin and a few hyaline and fine and coarse granular casts; the specific gravity had a tendency to be low and fixed, as shown by the test meal for renal function and the daily urine specimens as well; the phenol-sulphonephthalein excretion was 22 per cent in 2 hours, the urea nitrogen of the blood 35 mgm. per 100 c. c., and Ambard's coefficient of urea excretion 0.17. All the peripheral arteries were moderately thickened; ophthalmoscopic examination was negative except for somewhat tortuous arteries; the systolic blood pressure varied between 170 and 160 mm. of mercury, the diastolic between 100 and 90; the heart was slightly enlarged to the left, the apex beat being in the fifth space, 11.5 cm. from the median line. The final clinical impression was: Arteriosclerosis, primary contracted kidney of fairly advanced degree, hypertension, renal glycosuria, and possibly a mild diabetes mellitus.

TABLE IV.
BLOOD-SUGAR DETERMINATIONS AND DEGREE OF GLYCOSURIA AFTER 100 GM. OF GLUCOSE IN S. B.

	Fast-ing.	After 100 gm. of glucose.							
		15 min.	30 min.	45 min.	1 hour	1 hour 30 min.	2 hrs.	3 hrs.	4 hrs.
Blood sugar, %	.10	.15	.18	.23	.26	.26	.23	.10	.07
Urine glucose, %	.13	.13	.37	.80	1.61	3.33	2.00	1.11	.33

There is a distinct lowering of the kidney threshold for glucose, and a marked exaggeration of the blood-sugar curves both as regards the level to which it rises and the duration of the hyperglycemia. This, therefore, is a case of renal glycosuria, associated with chronic nephritis (see clinical data), and possibly diabetes mellitus as well.

The conclusions in regard to this case are that this is an instance of increased renal permeability to glucose, associated with a distinct nephritis, and possibly with diabetes mellitus as well. One final factor must be considered in explaining the varying intensity of glycosuria under apparently constant conditions. The reaction of the blood sugar to meals in any individual is not constant. Graham²³ attributed such changeable

²³ Graham, G.: Jour. Physiol., 1916, I, 285.

findings in health to fatigue. Similar variations occur in diabetics for no apparent reason (Table V). A more marked glycosuria would be expected to follow a blood-sugar curve such as is shown on December 1st than on either December 8th or 15th. The cause for these changing results is not clear, since this patient was on a carbohydrate-free diet of 1700 to 2000 calories for some time before as well as during the observations. Furthermore, the initial blood sugar was always taken while the patient was fasting, that is, before breakfast, and the meal was identical in each instance.

TABLE V.
BLOOD-SUGAR DETERMINATIONS IN A CASE OF DIABETES MELLITUS, AFTER A CARBOHYDRATE-FREE MEAL OF THE SAME WEIGHT AND KIND OF FOOD IN EACH INSTANCE.

Date.	Blood sugar per cent.													
	After a carbohydrate-free meal, of the same weight and kind of food on each date.													
	Fasting.	14 min.	15 min.	25 min.	32 min.	46 min.	50 min.	1 hour 15 min.	1 hour 19 min.	1 hour 30 min.	2 hours 2 min.	2 hours 33 min.	3 hours 5 min.	3 hours 30 min.
Dec. 1.....	.177	.180225225192161
8.....	.173142180
15.....	.072065065090	.086094110	.106

The results are very unlike each other, although this patient was kept in a small ward in the hospital during the period of study, under constant conditions of diet and hygiene.

Although these few experimental data do not exhaust these subjects, which are still under investigation, they show that the renal threshold to glucose undergoes great changes, and that the rise of sugar in the blood after meals differs greatly at intervals under apparently similar conditions. It is believed that these two factors, in addition to those previously mentioned, are largely responsible for the changing level of the D:N ratios often noted in well regulated cases of diabetes.

CONCLUSIONS.

1. The data of a case of diabetes mellitus demonstrating a maximal dextrose nitrogen ratio of 3.65:1 are presented.
2. Among the principal causes for apparently spontaneous changes in the D:N ratios present in some cases of diabetes mellitus are: (1) the inconstant renal threshold to the blood sugar, and (2), the variable heights to which the blood sugar rises after meals, even though these are not appreciably modified from day to day.

THE NATURE OF RESISTANCE TO TUBERCULOSIS.¹

By ALLEN K. KRAUSE, M. D.

(From the Kenneth Dows Tuberculosis Research Fund of the Medical Clinic of The Johns Hopkins Hospital.)

As our insight penetrates deeper and deeper into recesses that were once dark to us we consciously or unconsciously demand more precise description of terms to denote phenomena that obtrude upon our senses, but defy our under-

standing. Upon first appreciating a thing, be it light or sound, an abnormal sensation or an unusual conformation of the body, we give it a name. But we are mentally so endowed that we are not long content with the mere name of a thing. We must know where and how it begins and ends, and through what media it works: we must discover its attributes and, these determined, we must enlarge and refine our definition

¹ Read before the Academy of Medicine, New York City, February 15, 1917.

and description. With more precise definition and description comes the conception that nothing that we sense is isolated or autogenic. It is born of something and brings forth something. And once our minds begin to deal with its causes and effects then we can say that the thing has entered into our understanding. Then only can we affirm that its name is to us perhaps something more than a mouthful of words.

Terminology, description and a knowledge of cause and effect—every domain of knowledge, every phase of science passes through these three stages on the road from sensation to reason; and medicine, the all-embracing, the focus of all sciences, the handmaid of mathematics, physics, chemistry, botany, climatology, sociology and psychology, is to-day perhaps in all three stages. A genius, a Helmholtz, arises and lays bare the mechanism of the eye. A Richard Bright, a Louis or a Gerhard sifts, describes and clarifies a confused *mélange*. A man with a knack for observation, perhaps a dermatologist, classifies those things that are red, or those that are raised, or those that itch, or those that appear on certain parts of the body: and he thereby really brings under control his science and takes a step far beyond the time when he called everything a "humor" or a "tumor." But terms, mere terms, persist, and are too often accepted as explanations. Nephritis, cardio-nephritic, myocarditis, arteriosclerosis, hypertension, hypertensive-nephritic, myocardial insufficiency with hypertension, hypertension with renal insufficiency: what a real evolution of knowledge these terms convey, yet how little more than terms they are! Naming much and describing some things they explain nothing.

I feel very diffident in coming before you to-night and talking about what has often seemed to me to be, as commonly used, a mere term or symbol. I have attended clinics given by some of our best men and have heard the affirmation that a liberal diet of milk and eggs would increase the tuberculous patient's resistance. I have seen the specialist impressively produce his syringe and just as impressively assure the patient that a prolonged course of tuberculin therapy would further the latter's resistance. Time and again I have read that a man overcame his tuberculosis because his resistance improved or that he declined because he had no resistance. And hearing these statements I have often wondered just what was going through the man's mind when he talked about resistance. Did he mean anything or, if he did, had he any conception of what he tried to express? Or did he merely wish to avoid mental exertion and therefore seek to explain an effect by a handy word?

If there is such a thing as resistance to tuberculosis, then we must mean that the human body can protect itself in such a way that the tubercle bacillus, a parasitic invader, can gain no foothold or make but limited headway in it. We must assume further that under the influence of a specific irritant, the bacillus, the body reacts in a particular manner. So long as it reacts sufficiently to prevent the invasion or spread of the tubercle bacillus just so long we would say that resistance is satisfactory. If, however, it fails to do so, then resistance is lowered or absent. The entire relation of the tubercle bacillus

with the animal organism is one of reaction. *Vivre c'est réagir*: to live is to react; and from conception to final dissolution man's vital history is nothing but an unceasing period of countless myriads of reactions that go on simultaneously or unfold themselves in sequence. We must look upon every reaction to a potentially harmful stimulus or irritation as an effort at protection and adaptation. The body reacts to the rays of the sun in a certain definite manner and thus protects itself against them. It reacts to the introduction of pork or morphine in wholly different ways and thus adapts itself to them. It reacts to the implantation of the tubercle bacillus in a very particular manner and meets the germ with the formation of a special type of cellular accumulation which we call the tubercle. These are trite though fundamental conceptions of biology. In thinking of any tissue or organic attributes like resistance we dare not forget them, and it is likely that during the next few minutes I shall recur to them again and again. To live is to react. And, if the stimulus or irritant be one that is disagreeable to tissue, then to live is to resist. Whether resistance to a given irritant at any given time is adequate enough is another matter, yet it is certainly true that if we are to live, then we must resist. Therefore, in addition to the three necessary attributes of assimilation, motion and reproduction, as they are generally given for protoplasm, I would add a fourth attribute, resistance. I am aware that this fourth attribute may be partly contingent on others such as assimilation and motion, but it is conceivable that in highly organized animals resistance goes on independently of them.

We assume, therefore, that there is a resistance to the tubercle bacillus, but in thus stating the proposition we have got little beyond giving a name to the known fact that tissues react to tubercle bacilli. We have not explained or illuminated a single thing. It is my purpose to-night to inquire into the nature of this resistance, to attempt to discover how it acts and what are its effects. I trust that you will be tolerant with me while I lead you into regions which, I know only too well, are strewn with obstacles and beset with pitfalls.

Let us first look into what happens when tubercle bacilli are taken into the body for the first time. Let us take for granted what happens in the vast majority of cases, that is, that they enter by the mouth or the nose. After excursions of varying lengths they come to rest. They may be caught in the vibrissæ of the nose, on the moist surfaces of the tortuous nasal passages or in the mucus of the nasopharynx, and be almost immediately blown out or expectorated with the nasopharyngeal secretion. Here at the very beginning we meet with a protective mechanism at the body's command.

But let us assume that they get further and penetrate the mucous membrane of the tonsil or pass into the submaxillary glands or go further down into the larynx and reach the deep cervical glands. They are now no longer *on* an epithelial surface where they cannot produce an effect: they are *in* tissue. What happens now? The tissue reacts. Fixed tissue cells of connective tissue (mesoblastic) type begin to show agitation and unrest. Their nuclei swell, chromatin rearranges itself

and heaps up in a bizarre manner, the cells themselves enlarge and in a short time we find that they are dividing, multiplying and heaping up, and surrounding and englobing the offending parasites. Now, too, cells begin to slip in from the circulation. Leucocytes accumulate in this new, round, globoid speck of matter and a tubercle comes to view. A few more days go by, and we meanwhile study the life cycle of this tubercle from time to time. What do we find? We notice developing under our eyes an avascular growth or formation of tissue, surrounding and englobing the parasitic invaders and shutting them off from the rest of the body. The bacilli are held within a globular, bloodless wall. So long as the wall is competent, so long as circulation between the interior and exterior of the tubercle is at a minimum, so long as the fibrous wall of the tubercle holds against invasion by bacilli from within or a flooding of body fluids and a consequent softening from without, just so long will the body have the germs in this initial tubercle under control.

Fortunately for most of us this is the extent of our more intimate and involuntary acquaintance with the tubercle bacillus. We are infected but without clinical disease. We have tubercle but not tuberculosis. And once having tubercle, it may be that with never a symptom of specific illness we will go through a long life without ever thoroughly eradicating the tubercle bacilli from our bodies. Though this statement cannot be proved, all our knowledge points to the fact that once having gained entrance to an animal body and once having developed sufficiently to arouse tubercle, the bacilli are never completely wiped out. Why, then, when all of us are infected, are so few of us ill? Where does resistance begin, what does it consist in and how far does it go? For surely there must be some resistance, or otherwise the bacilli would multiply and spread through us like wildfire. Under the very special premises that I have outlined, is there a resistance to infection or implantation or is the resistance merely to subsequent invasion? Has any man or animal a native resistance to initial infection by a type of tubercle bacillus to which his kind is susceptible?

We know that several diseases do not decimate civilized communities in the way in which they cut down primitive peoples. Measles and tuberculosis are real plagues if introduced among the Esquimaux and the dwellers of the South Sea Islands, but to-day occur as relatively benign diseases among peoples who have a long history of community life behind them. For this reason we postulate and teach that some nations have developed a racial immunity to tuberculosis and measles. This may be true to a certain extent, but this racial resistance is not a resistance to infection. If exposed, practically every child on earth to-day develops measles and practically every human being reacts with tubercle. In other words, all become infected; and we cannot assume that there is any racial resistance to implantation of the micro-organism. Again, if an individual is not tainted with tubercle, we cannot by any known method demonstrate that he harbors substances that may be antagonistic to the tubercle bacillus. And, if we treat an animal by certain

procedures we may find in his blood certain bodies like agglutinins, aggressins, precipitins and opsonins, yet unless we give the animal anatomic tubercle it will not be more resistant to infection than any other non-infected animal that has not been thus treated. Because of these facts we must assume that man and animals have no native racial resistance to infection by tubercle bacilli in the sense that born in them is some substance or substances that specifically destroy or neutralize tubercle bacilli that seek an entrance. But there is a difference between the way in which the tissues of the Jew meet the onslaught of the tubercle bacillus and that in which the tissues of the Esquimaux meet it. There is a difference between the reaction of the tissues of the new-born infant and those of the city-dwelling adult to bacillary implantation. Both the time and character of these reactions are different. The tubercles develop differently and this difference of development in large part determines the issue. Remember that tubercle formation is response to irritation, be the irritant a hair, a grain of sand or a living, self-propagating, parasitic tubercle bacillus containing, as it does, a very high percentage of fats and waxes that are got rid of by the body only with great difficulty. This reaction is resistance, and an attempt on the part of the body to isolate or wall off the foreign body. Remember that, inasmuch as all of us become harborers of tubercle, we must assume that there is no native *increased* resistance to infection by tubercle bacilli. Remember, too, that as tissues become infected their capacity to react changes.

Let us now consider for a moment what I choose to call the mechanical element in resistance to tuberculosis. I have often wondered why pathologists have not paid more attention to the architecture of the tubercle as a formation designed by its very structure to resist further invasion by the tubercle bacillus. To me the most impressive feature of a tubercle is the fact that here we have a wall built around a foreign body, that the wall is formed around the foreign body to encyst it and render it innocuous to the infected organism, that, as long as the wall holds, the germs cannot get out and spread throughout the organism and that a necessary condition to the competence of the investing wall is fibrosis and a minimum of circulatory give and take between the center of the tubercle and the tissue that surrounds it. We can go even further. We can affirm that to produce symptoms of disease the tubercle must give up something in itself to the body, that the latter must absorb this material if it is to suffer symptoms of illness, that it can absorb something from the tubercle only if there is again a sufficient circulatory give and take between it and the tubercle, and that the circulatory exchange between tubercle and infected organism will be directly proportionate to the degree of fibrosis or sclerosis of the investing wall. Thus, resistance to further spread of bacilli and freedom from symptoms are to be understood not in terms of the body producing some fighting units which go out to battle with the germs or to neutralize their poisons. They are to be understood as being simply the result of a mechanical barrier which the body interposes between itself and the parasite.

Suppose a man has such a tubercle in his lung in close proximity to a blood vessel. It has never made itself manifest. The man has always been in perfect health. In perfect health he runs a hard race or plays a fast tennis game. Like a bolt from the sky a pulmonary hæmorrhage strikes him down, and immediately he falls ill. Another man leaves home in the morning feeling perfectly well. Suppose that for years he has had a slow and sluggishly progressive tuberculous process in a bronchial gland, yet has never had a symptom from it. Suppose further that while he is at his desk the last tenuous sheath between this caseous gland and the lumen of his bronchus is broken through, perhaps because of coughing or some sudden muscular effort. And suppose that the contents of this diseased gland are discharged widespread into the bronchus. Such a man comes home in the evening sick, with beginning caseous pneumonia.

Suppose now that for years a small gland has lain close to the thoracic duct and that firmly shut within its capsule there has smouldered tubercle. But the time comes when the tuberculosis ulcerates into the thoracic duct and from perfect health a man is precipitated into generalized miliary tuberculosis.

What shall we say about such patients? Shall we say that they developed acute tuberculosis because their resistance gave way? Yes, we may say so. But what did their resistance consist of? In these cases resistance certainly meant that foci of infection and disease were isolated and shut in by barriers of tissue and that when the barrier went resistance went.

Let us take another instance. Here is a tubercle in the lung, with bacilli well shut in and wall thoroughly competent under ordinary conditions, and its possessor a thoroughly healthy man. He develops a common cold or a bronchitis and soon after presents symptoms of tuberculosis. In terms of resistance how shall we view the onset of his tuberculosis? I have often heard just such cases explained in terms something like this: that the acute respiratory disease lowered the man's resistance, that he was left in a run-down condition, that the cells of his body therefore lay more open to invasion by the tubercle bacillus. I shall not pay detailed attention to the lack of precise reasoning in such an explanation. But I should like to put forth one that is much more plausible, and, I believe, deals more with physiological facts. Is it not more likely that during the man's "cold" or bronchitis there was a certain amount of congestion of the affected tissues, that this congestion extended to the neighborhood of the tubercle and that it established new channels of communication and circulation between the tubercle and the surrounding tissue, unlocking or opening the capsule and allowing a fresh dissemination of interned bacilli? If hard exercise will produce the circulatory conditions necessary to break through an old tubercle and thus cause unlooked-for hæmorrhage, why will not congestion about a tubercle exert a more or less similar effect? Here again resistance is a matter of simple mechanics. The patient is as resistant as the shell of his tubercle.

Hard physical exercise, sudden and intense muscular exertion, a cough, a common cold, childbirth, tuberculin in overdose, alcohol, all can produce the same circulatory effect in the neighborhood of the tubercle and, theoretically at least, can bring about the same result, a better circulatory give and take between the tubercle and the host, with a recrudescence of symptoms or a mobilization of bacilli or both. This may be momentary or it may be prolonged. If the inflammatory stimulation is not overdone, proliferation and repair will soon set in, and good may result. If it is too intense, then dissemination and progression of disease may ensue. But there is no doubt that some part of what we have been accustomed to call resistance to tuberculosis is more or less bound up with the mechanics of the circulation around the tubercle.

The body responds to exercise in a very definite way: the pulse rate and pressure rise and the respiratory activity is increased. It is not difficult to imagine how under these circumstances the lungs are affected and what might happen to an old encysted tubercle. We recognize this fact in treatment, particularly when we warn our patients to suppress cough as much as possible. By complete rest we put the lungs in as complete circulatory inactivity, relatively speaking, as possible; and we do raise the patient's resistance, but we do this in a mechanical way by striving to avoid any maneuver that will enhance the circulation in the lung and in the tissue around the tubercle.

Consider, too, the accidents that must modify the course that tuberculous infection and disease are going to take. In our struggle to attain definite rationale and generalization in medicine, I sometimes think that we are all too prone to forget the large part that accident plays in the development of a pathological process. A man may have vegetations on his heart valves and these may be continually shed off and lodge in skeletal muscles and no harm result. But another man with an identical cardiac condition may drop dead because the first embolus that breaks loose is swept into his coronary artery. Similarly, accidents undoubtedly determine the course of tuberculosis. It surely makes a great deal of difference whether the first infection in the lungs develops near the pleura or near the hilus or near a large blood vessel or at the apex. The brain is not the only organ of the body that has its silent areas and its eloquent areas. The lungs have theirs too: and the effect will be not so much a matter of resistance as of location. To say that a man who had a caseous gland that erupted into the thoracic duct got generalized miliary tuberculosis because he lacked resistance to tuberculosis, would be just as foolish as to affirm that a man who dropped dead, lacked resistance to coronary embolism.

Besides the accidents of place or location, there are the accidents of time. A great deal may depend on just when a patient develops an intercurrent infection, such as an acute bronchitis, or suffers unusual physical strain. The same episode in his life may produce very different results. It may occur when the concealed tubercle is thoroughly sclerotic and therefore completely withstands the changed anatomical or physiological processes going on in its neighborhood. Or it

may occur at a time when the investing wall of the tubercle has just the proper structure to establish fresh communications with the surrounding tissue under the right conditions. Perhaps this is why young children, if compared with adults, withstand stress and infections relatively poorly so far as the effect of these on quiescent tubercle is concerned. Their tubercle is of comparatively recent origin, is not completely fibrosed or healed and is thus much more open to assault. As they grow older this healing process has advanced further and further, so that we say that in regard to tuberculosis, five to fifteen years is the golden age of man's span. But once having passed puberty they enter a period of from 15 to 20 years when life's stresses are at their maximum and the increased mental and physical strain in many cases produces local effects that are more than even healed tubercle will bear. I say "healed" tubercle with some mental reservation. I would have you recall that living tubercle bacilli have been found in the chalky deposits of tuberculous areas that had healed by calcification. It is for these reasons that I am very fond of telling our students that the development of tuberculous disease from old benign tubercle depends largely on whether the patient gets a cold or rows a race or becomes pregnant at the wrong time.

We have thus far discussed the protective reaction by which the tissues seek to hem in and wall off the first tubercle bacilli that gain entrance to the body and exert their effect upon them. We have also considered local conditions by which the infected organism resists the development of tuberculosis. We have looked upon the tubercle as a growth the periphery of which acts as a barrier to the egress of bacilli and yet is subject to all the physiological disturbance that goes on around it. We have seen how the permanence of benign tubercle or the conversion of benign tubercle into tuberculosis will depend largely on the mechanical interaction and balance of these opposing factors. Let us now extend our line of reasoning to an inquiry into conditions in the patient who presents himself to us with active tuberculosis.

Such a patient, of course, has anatomic change and he has symptoms. Why has he symptoms? Because he is absorbing something from his foci of disease. Why does he absorb something? Because there is a sufficient circulatory give and take between his foci and the surrounding tissue. Why is there this circulatory give and take? Because the walls, the envelopes, the investments of these foci are not competent to block off the interior of the tubercles. If, in course of time, these walls become more and more fibrous and more and more impervious, the severity of the patient's symptoms will surely diminish. This fact is so obvious that I consider it hardly necessary to enlarge upon it. Whether by design or not, we recognize this principle in treating our patients. If they are symptomatic we put them at rest in order to quiet the circulation and respiratory activity. Under such conditions they may be without symptoms. If now we allow them to exercise again symptoms immediately recur. Now their relief from symptoms, their resistance to symptoms, cannot be due to any neutralizing substance which the body elaborates, for, if it is,

then we should not expect this prompt response to rest and exercise which by their action on respiration and the circulation we know simply diminish or increase the opportunities for absorption. You have all had patients with incipient tuberculosis who suffered markedly from symptoms of absorption and who, upon the ulceration of their process, informed you that they felt a great deal better. Here by ulceration Nature has applied the prime surgical principle of more or less thorough evacuation of a focus of disease.

The point I want to make is that the presence or absence of symptoms is to a certain extent contingent on focal mechanics. I think we can say absolutely that increasing fibrosis means a gradual release from symptoms; whereas increasing softening without coincident and sufficient peripheral fibrosis means added severity of symptoms. The man who has extensive anatomic tubercle with comparative freedom from symptoms has his tuberculous areas well sclerosed and hemmed in. The man who has but slight anatomic change with marked constitutional disturbances has but very slight investment of his focus. Whether this mechanical element is all that there is to resistance to symptoms I am not prepared to say, but it certainly plays a very large part in resistance.

And, so far as extension of anatomic change is concerned, you can neglect all other factors and assert almost dogmatically that so long as fibrosis is the predominant element in any particular case, just so long are fresh eruptions much less likely to occur than if degeneration and exudation gained the upper hand. Apart from any native or acquired habit of bodily constitution which, in a vague way, we are pleased to call resistance, purely local mechanical conditions play a very large part in resistance to tuberculosis, whether against first infection or against subsequent eruption.

I am, of course, aware that you are all saying, "Yes, but what determines fibrosis and caseation, degeneration and repair? Is it not possible that there is an underlying resistance, a native or acquired attribute of the animal body, that confers upon the tissues the ability to react in such a manner that ideal fibrosis is attained?" Yes, it is not only possible but highly probable; and it is to this phase of resistance that I wish to address myself during the remainder of our inquiry. The manner in which tissues react determines resistance. Let us now examine the probable factors that determine or influence the reactions of tissues. Let us study the reaction of tissues to irritation in general and to the tubercle bacillus in particular.

I take it as axiomatic that individuals vary tremendously in their reaction to irritation. This ability to react in varying degrees is certainly to some extent congenital. Stimulated by the same irritant, one man's cells will over-react while another man's will hardly respond at all. In this connection, Maud Slye's work is of tremendous significance. She works with two large series of mice. The one series consists of animals that have never had cancer bred into them; the other, of those which she is continually fortifying with a cancer heredity by mating their progenitors with individuals of known cancerous stock. She finds that individuals of the

cancer strains react very differently to irritation than do those of clean stocks. If injured, many will develop cancer at the site of the wound whereas none of the non-cancerous strain ever reacts with cancer under the same conditions. Many of the latter, however, become ill with the ordinary infections and die. In cancerous strains, infections are very unusual and, if they occur, are resisted well. She would therefore generalize about as follows: Cancer is the result of a congenital tendency to over-reaction to irritation. Animals with this tendency do not easily acquire infections. If they do develop them, they resist them well. Infections strike down the weak. Cancer attacks the strong.

If Maud Slye's work is sound what shall we say? Shall we conclude that it is possible that the same tissue tendency that is responsible for cancer also protects against infection. Shall we assume that the irritant, the parasitic micro-organism, gains slight foothold or none at all because it is immediately met by an exaggerated effort on the part of the body cells to ward it off? I am here reminded of a remark which that wonderfully keen observer, Dr. Trudeau, repeatedly made—that cancer was a disease of the strong, progressive tuberculosis a disease of the weak. He undoubtedly based this observation on his impression that so many people who developed cancer gave histories that were relatively free from infection during early life. I do not wish to develop this particular phase of the subject further. The point I would ask you to remember is that individuals do vary in their response to irritation, that this response may take the form of an over-reaction, an overgrowth, an over-production of tissue, that evidence is coming in that in some of us this tendency is inbred and that the same mechanism that resists infections may lay us open to cancer if the proper irritation is at work.

If any foreign body that is not assimilable gains access to the body, the tissues react in a characteristic way, that is, with the formation of tubercle. Similarly, tubercle bacilli which are more or less non-assimilable by the tissues, incite the formation of tubercle. Now there are several things that will modify the type of reaction that sets in against the irritant. One is the number of infecting bacilli. Long ago Baumgarten pointed out that, if the bacilli were few, the reaction would be manifested by the proliferation of only one type of cell. If only a few bacilli lodge at a point, then for a number of days the only reaction which we note is a proliferation or renewed growth of those cells which we designate as belonging to the fixed tissue type. The resultant structure is a tubercle that has all the features of a tumor and none of the essentials of an inflammation. Such a tubercle may be made up of cells of the connective tissue type alone. There may not be a leucocyte or any other element of inflammation or exudation in it. Here we have really a growth or new growth or tumor comparable to what under ordinary circumstances we would call a fibroma.

If, however, the initial number of tubercle bacilli is large, the first reaction is an outpouring of polymorphonuclear leucocytes. But within an hour the fixed tissue cells begin to

show signs of unrest, and proliferate. The polymorphonuclear leucocytes soon disappear and tubercle formation goes on characteristically with a gradual inwandering of lymphocytic cells which distribute themselves throughout the mass of fixed tissue cells, which in this location have come to be known as epithelioid. We see, therefore, that under ordinary conditions the body reacts to first infection in a variable manner according as the irritation is more or less intense. But the reaction is very regular and definite and, if the infecting bacilli be the first that have gained access to the body, the result will always be the same. The reaction to first infection will always eventuate in the production of *focal* tubercle. The relative proportion of leucocytes and epithelioid cells in different tubercles may vary, but the resultant response to first infection will always be focal. The tubercles will be very definite, isolated and discrete formations, with bacilli near the center and concentric layers of epithelioid cells interspersed with leucocytes forming the periphery. And as we look at them we think of the wall or barrier about which we have said so much. These reactions go on in a perfectly orderly manner. Microscopically, they begin to be evident a few hours after inoculation if ordinary doses of bacilli are used: macroscopically they present themselves to view from about the eighth to the tenth day on. Meanwhile the guinea-pig or rabbit does not exhibit the least symptom of constitutional disturbance from the time the first inoculation is made until the fourth or fifth or sixth week when the disease is progressing rapidly throughout the body.

But note that what I have described applies only to the results of a *first* infection with tubercle bacilli. If I wait until these initial tubercles develop and then reinfect my animals I may get a response of a totally different character. We may watch this response very prettily if we perform our reinfections in the skin (intracutaneously) which we can always keep under observation. We then find that there is an immediate reaction to the reintroduction of tubercle bacilli. Four or five hours after reinfection the tissue at the point of infection begins to inflame. This acute inflammation progresses and after 24 or 48 hours may be marked, both in extent and intensity. It then subsides and a few days later anatomic tubercle begins to develop in the spot. But it develops differently than did the tubercles aroused by the first infection. It appears earlier and has an accelerated development and soon subsides. And unless the reinfecting dose was overwhelming the reinfection may get no further than the skin. In other words, the reaction which we now get is comparable to what we observe when we reinoculate vaccine virus into a person who not long before has had a vaccine "take" or if we reinoculate an animal that has a chancre with a fresh dose of syphilitic virus. The reaction is accelerated and abortive and partakes more of the nature of a pure inflammation, though this latter feature will depend largely on the size of the reinfecting dose.

We are here dealing with a very striking phenomenon, the importance of which is just beginning to be generally recog-

nized. We may pause here for a moment to generalize and say: that the development of anatomic tubercle in the body, consequent upon the introduction of tubercle bacilli, so changes the body that all its tissues react entirely differently from the normal to the application of any soluble protein products of the tubercle bacillus or to the reintroduction of living or dead tubercle bacilli.

Everyone of you has become more or less familiar with this type of reaction in your application of the various cutaneous tests to detect tuberculous infection. And if you have followed the experimental and clinical observations that have been made on this reaction you have learned: 1. That the reaction occurs only when anatomic tubercle is present somewhere in the body. 2. That the reaction begins to manifest itself with the establishment of tubercle. 3. That up to a certain point, as the tuberculous involvement or disease progresses, the intensity of the reaction increases. 4. That as tuberculous disease heals, the intensity of the reaction tends to become less and less. 5. That inasmuch as tubercle is perhaps never entirely eradicated from the body, the power to react is probably never completely lost. These facts are as certain and as easily demonstrable as any that we know concerning tuberculosis. When we formulate them, we are not indulging in the least bit of speculation. And we would state it as a law that the development of tubercle endows the animal body with a capacity to react against the tubercle bacillus or any of its products which it did not possess before. We would go further and state that not only the skin, but all the tissues of the body, the pleura, the peritoneum, the lungs, the liver, etc., take on this changed capacity to react. And we would also recall that no one has yet succeeded in obtaining this changed reactivity in an animal unless he first gave the animal a focus of tuberculous infection.

But with the development of anatomic tubercle other deep-seated changes also take place in the animal body. For 20 years it has been recognized that an animal with tubercle can withstand relatively enormous numbers of living virulent tubercle bacilli as compared with a normal animal. For 20 years and more the details associated with this phenomenon of acquired increased resistance have been studied and the results of these studies may be summarized as follows: 1. The development of anatomic tubercle endows the body with the power to resist greatly increased numbers of tubercle bacilli. 2. This increased resistance to infection manifests itself with the establishment of the first foci. 3. Up to a certain point, resistance is directly proportionate to the extent and severity of the initial disease. 4. With the healing of the diseased foci, resistance diminishes. 5. If the animal remains tuberculous, the increased power to resist is probably never entirely lost, nor does resistance sink to the level which obtained before the animal was first infected. Furthermore, so far as resistance is modified by the introduction of tubercle bacilli or any of its products, this increased resistance can be obtained only by making the animal tuberculous, that is, *by inoculating the*

animal with tubercle bacilli. It is true that non-tuberculous animals may be treated with tuberculins of various types and that because of such treatment their serum may contain such bodies as agglutinins, precipitins and opsonins, but such animals are not resistant to infection as compared with normal, non-tuberculous ones. We therefore assume that the ordinary serological antibodies that are met with in tuberculous infection have no direct connection with resistance to infection. In short, when we consider the effects of the tubercle bacillus and any of its products, only the tuberculous animal has a relative immunity to tuberculosis.

For a number of years several of us have been studying this changed reactivity (hypersensitiveness, allergy) and this increased resistance of tuberculous animals. We have never failed to be impressed by the points of contact that the two phenomena exhibit. We have, therefore, wondered whether there was any close or direct relationship between the two. We have thought it reasonable to speculate that perhaps resistance to infection dwelt in this capacity of the tissues of a tuberculous animal to react immediately in an inflammatory manner. It might well be that this initial acute inflammation and the subsequent accelerated development of tubercles took care of the invading bacilli in a more satisfactory manner than did the tissues under ordinary normal conditions. For here the tuberculous animal responds with exaggerated or over-reaction to irritation and throws up a barrier against the bacilli much more actively than normally, and before the bacilli can get under way. From the point of view of the effect of pure inflammation we had some warrant for our belief. Pawlowsky had already demonstrated that if he first inflamed a guinea-pig's knee-joint with a sterile irritant such as turpentine, alcohol or quinine, staphylococci which he then introduced into the joint would not disseminate beyond it, although 24 to 48 hours after the injection of staphylococci into a normal joint, he could recover the micro-organisms from the blood and organs of the guinea-pig. Isayeff had also shown that "the peritonitis induced by a variety of sterile irritants such as a foreign blood serum, bouillon or normal salt solution, temporarily increases resistance to subsequent intraperitoneal inoculations of bacteria." We have therefore done many experiments to validate our view. I regret that to-night I cannot bring to you absolute and definite proof that increased resistance to infection is bound up in and dependent on over-reaction or hypersensitiveness of tissue, but I think that I do not go too far in saying that all the facts point that way.

We can inoculate normal guinea-pigs or rabbits subcutaneously in the groin with a good dose of a more or less virulent strain of tubercle bacilli. After several weeks we find that glandular swellings are developing in the groin and that at the same time the animals' skins are hypersensitive to tuberculin. We can now inoculate such animals intravenously with large quantities of a virulent strain and at the same time inoculate normal animals in a similar manner. The normal

animals do not suffer the least inconvenience or immediate symptom from the inoculation. But within a few hours the reinfected tuberculous animals fall ill and from within 12 hours to four days many of them may die if the dose has been large enough. Those that do not die gradually recover from their acute illness and, as a rule, live on for months and many of them for a year or more, never dying of tuberculosis.

If we section the animals that have fallen acutely ill and have died shortly after reinfection we find that their lungs exhibit areas of hæmorrhagic exudation or acute pneumonia or œdema which we find is the result of tubercle bacilli lodging in already sensitized soil which has over-reacted. Controls sectioned at the same time, up to about eight or ten days after infection, never show these acute pathological reactions. We find, therefore, that animals which we know have increased resistance as well as increased tissue reactivity develop symptoms of illness while they over-react, and we also find that in response to reinfection their tissues react in a particular manner as compared with what occurs after the first infection. The character of the reaction, if the number of organisms at any point is sufficiently large and if the tissues have a very high degree of hypersensitiveness, is exudative or inflammatory, resulting in areas of pneumonia or congestion. A first injection of tubercle bacilli, you will remember, never produces such an effect. It excites the body to react only with focal tuberculous change, never with a diffuse process. Remember, however, that I am speaking always of what occurs as the immediate result of the first infection. Remember that a first infection will sensitize an animal after it has progressed for from 10 to 15 days on, and that then any extension of this infection will occur in hypersensitive soil. At any rate, as a result of such experiments we would postulate that the diffuse types of tuberculous lesion, the pneumonias, the pleurisies with effusion, the hydrops of joints, can occur only as the result of reinfection and never upon first infection and that the result of first infection is always a focal, invested tuberculosis. If the reinfesting dose of bacilli is small, then the lesion may also be focal, but the foci develop much more rapidly than upon first infection and they are abortive and tend to disappear.

You see, therefore, that, beginning with a study of resistance to tuberculosis, we are rapidly drifting into the realms of pathology and symptomatology if we pay attention to the wealth of observations that this study of resistance serves up to us. For the first time we can attempt to explain on a solid footing the tremendous variety of lesion that the tubercle bacillus produces in the body, a pathological result that has puzzled and confused observers since autopsies were first performed. As a rule we can affirm that it is the bacillus that is the constant and the animal that is the variable. I can take the same emulsion of the same bacillus and use the same dose to inject a series of animals. If the animals are normal I always obtain the same early result, focal tuberculosis. But if the animals are already tuberculous then almost every

variety of lesion is likely to occur and the type of lesion will depend on two factors: on the number of micro-organisms brought to bear at any one point and the degree of hypersensitiveness or over-reaction of the tissue at this point.

Again, we note that symptoms of acute illness occur only in reinfected animals and never in the controls. This suggests what is probably true, that acute tuberculosis never develops as a first infection, that it is acute because it is more of the exudative type and that its exudative type and the acute symptoms are simply expressions of resistance, of over-reaction, of immunity, of hypersensitiveness, call it what you will.

I wish I had time to develop this phase of the inquiry for, as a rule, I find myself growing unaccustomedly eloquent in examining the relationship of resistance to the pathology and symptomatology of tuberculosis. But I have perhaps already taken too much of your time and, like the best writers of fiction, shall close the story by suggestion.

Yet I cannot close without taking this opportunity of making a plea that all who have a lively interest in resistance to tuberculosis, to syphilis and to other infections and to cancer, study these problems from the angle of tissue reactions to irritation. The field is tremendous and has hardly been scratched in a systematic way. We must study the biology of these pathological formations in a developmental manner from the first signs of reaction to irritation right through to ultimate loss of tissue. For many years our pathologists have studied finished tuberculosis as they encountered it at autopsy and only too often have sought to unravel our most difficult problems by meticulous observation of cavity and cheesy patch. But the slender threads that hold the solution to the riddle have long been cut down in the cavity. What we need are careful anatomical and physiological studies of the relation of tubercle to its immediate environment; tubercle of all kinds, tubercle in all stages of development, tubercle as a first infection and tubercle as reinfection, human tubercle in the chicken and avian tubercle in the guinea-pig. What we do not know about tuberculosis almost staggers the imagination when we consider the time that has been spent on its study. How little we really and actually know about what happens after the bacillus has passed the lips and anterior nares! I would therefore appeal for workers in the field. No one man, no school, can discover it all, but if we work together then perhaps we may partially succeed in satisfying that intense longing which all of us have: really to *know* a little corner of our chosen study before we die.

NOTICE.

Owing to the great increase in the cost of all supplies, it has been found necessary to increase the subscription price of THE JOHNS HOPKINS HOSPITAL BULLETIN to \$3.00 a year. Single copies will be sold at 50 cents. This increase will take effect at once for all new subscriptions. Renewals will come under the new price as they become due.

THE AMINO-ACID NITROGEN OF THE BLOOD IN CASES OF NORMAL AND COMPLICATED PREGNANCY AND ALSO IN THE NEW-BORN INFANT.

By ARTHUR MORSE.

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Since the work of Fischer and of Kossel teaches that the protein molecule is composed of amino-acids, we assume that a close analogy exists between the synthesis of polypeptids in the laboratory and the synthesis of protein in the body. Moreover, it is natural to believe that fetal protein is built of amino-acids supplied from the mother's blood. From this standpoint a peculiar interest attaches to the blood of pregnant women, and several fundamental questions arise. We should like to know, for example, whether the maternal blood contains an unusual quantity of amino-acids during pregnancy? How does the quantity of these substances in the mother's blood compare with that in the blood of the fetus? And, in the presence of autointoxications, are abnormal values for the amino-acids encountered in either circulation?

With the Van Slyke method these problems may be profitably studied. However, it is still impossible to estimate the utilization of individual amino-acids by the fetus, as Mendel and Osborne have done in the case of young animals. Not unlikely, what they have found true for the nutrition of lower mammals applies equally to infants, and perhaps also to the preceding period of intrauterine development. But the Van Slyke method, of course, estimates the aliphatic amino-acids only in the aggregate; and others it does not estimate at all. This may not constitute a serious omission and may even prove to be negligible, when the problem is to learn what is the total quantity of amino-acid nitrogen in the blood. But it is noteworthy that some of the amino-acids which Mendel and Osborne have shown to be essential for growth are not included by the Van Slyke method.

Formerly, it was believed that the blood proteins could be satisfactorily removed by precipitation with colloidal iron, before undertaking the estimation of the amino-acid nitrogen; and consequently, in the first cases I studied, the plasma was so treated. For the sake of contrasting that method with the one later adopted, the earlier results are included in this report. But, generally, following the recommendation of Greenwald, a solution of 2.5% trichloracetic acid was used for protein precipitation. With this method higher values are obtained, for the precipitate does not appreciably absorb the amino-acid nitrogen sought in the later analysis of the filtrate. This technique has been adopted by Van Slyke and approved by others, most recently by Bock, who regards the values thus secured as nearly absolute.

The need of a standard with which to compare the values in pregnancy required observations upon normal women. As subjects, we selected patients entering the hospital for the repair of lacerations incident to childbirth, months or years previously, or others requiring a gynecological examination

which, however, revealed nothing abnormal. The results indicate that the blood of women contains normally from 8 to 14 mg.¹ of amino-acid nitrogen.

NON-PREGNANT WOMEN.

Number.	Para.	Age.	Amino-acid nitrogen.		Remarks.
			Whole blood per 100 c. c.	Plasma per 100 c. c.	
			mg.	mg.	Trichloracetic acid technique.
1	0	18	13.6	12.4	Normal woman.
2	I	26	11.5	8.2	" "
3	I	35	10.6	" "
4	IV	24	9.7	" "
5	V	50	8.6	" "

Because there was not a suitable method for direct determination of the amino-acids in the blood, until recently it was customary to calculate what this fraction of the non-protein nitrogen was. By subtracting the urea-nitrogen from the total non-protein nitrogen, Bang found in a series of 11 women from 6 to 17 mg. of amino-acid nitrogen. An error was involved, since the calculation did not take into account uric acid and creatinin; yet formerly the indirect method yielded more accurate results than direct determinations. For example, after precipitation of the blood-proteins with alcohol the analysis indicates only 5 to 8 mg. as normal; a very low result which, as was said, is explained by the absorptive action of the precipitate.

As normal values, 12 to 13 mg., which come within the range of my determinations, have been recorded by Rosenberg; and the same result was obtained by Gorchkoff, Grigorieff and Koutoursky, who also noted an increase of 3 to 4 mg. after meals.

PREGNANCY.

Number.	Para.	Age.	Amino-acid nitrogen.		Remarks.
			Whole blood per 100 c. c.	Plasma per 100 c. c.	
			mg.	mg.	Trichloracetic acid technique.
6	III	30	8.4	7.5	Second month.
7	V	40	8.9	Third month.
8	III	34	9.6	Fifth month.
9	II	28	14.2	Sixth month.
10	I	30	13.6	Eighth month.
11	III	32	10.9	At term.
12	I	30	10.7	8.7	Ninth month. Mitral lesion.

In the blood of pregnant women the amino-acids are not increased; generally, from 8 to 14 mg. are found, the normal

¹ Throughout the paper, the results are expressed in terms of milligrams of amino-acid nitrogen per 100 c. c. of blood, or of plasma, according to the material used for analysis.

range of variations. Among my cases lower values appeared at the 2d and 3d months than later, but this may not be safely ascribed to the period of pregnancy, for quite as large individual differences exist between non-pregnant women. On the other hand, there are several reasons for suspecting con-

MATERNAL VALUES IN TOXÆMIAS OF PREGNANCY.

Number.	Age and para.	Amino-acid nitrogen.		Remarks
		Whole blood per 100 c. c.	Plasma per 100 c. c.	
		mg.	mg.	Trichloracetic acid technique.
13	25	12.6	Pre-eclamptic toxæmia. Hydramnios, 7th month.
	I			B. P. 150, N. P. N. 32.5; Urea N. 19.1 mg.
14	20	15.3	Pre-eclamptic toxæmia. B. P. 170.
	I			Albuminuria 1.4%.
15	20	13.2	Ante-partum eclampsia. B. P. 155.
	I			Albuminuria 6%.
16	24	12.4	5.4	Ante-partum eclampsia. B. P. 180, albuminuria 1.5%.
	I			N. P. N. 47.9; Urea N. 15.9; Uric acid N. 9 mg.
17	38	(a) 17.9	Ante-partum eclampsia. B. P. 200, albuminuria 6%.
	VIII	(b) 17.9	(a) Cæsarean section. (b) 3 days post partum.
18	37	(a) 19.1	Intra-partum eclampsia. B. P. 200, albumin 2%.
	I	(b) 26.1	(a) Delivery, (b) 8 hours post partum, (c) 30 hours post partum.
		(c) 28.3	
19	33	10.3	Post-partum eclampsia.
	III			B. P. 180.
20	37	13.5	Nephritic toxæmia. Fourth month pregnancy.
	II			B. P. 255, albuminuria .4%.
21	37	8.8	Nephritic toxæmia.
	I			B. P. 250, albuminuria 4%.
22	26	7.1	Nephritic toxæmia.
	I			B. P. 190, albuminuria 2.25%.
23	20	15.1	Obscure toxæmia. Pre-eclamptic? No albuminuria.
	I			B. P. 180. Normal delivery. Amino N. of fetus 15.1 mg.
24	20	21.6	Obscure toxæmia. B. P. 155. No albuminuria.
	I			Normal delivery. Amino N. of fetus 21.6 mg.
25	18	21.4	Obscure toxæmia. Diacetic ac. and acetone in urine.
	I			B. P. 110, normal delivery. Amino N. of fetus 24.4 mg. No albuminuria.

sistently lower values in the earlier than in the later months of pregnancy. The former are often characterized by a relatively poor state of nutrition dependent upon loss of appetite, nausea and vomiting, while during the later months usually good health and an excellent state of nutrition are the rule. It is also true that the protein requirements of the embryo are notably less than those of the fetus. Perhaps, then, more extensive material may show a consistent difference between

the early and the late months of pregnancy, though from my results it may be said that the values in both periods are within normal limits. Evidently, therefore, the usual quantity of amino-acids in the mother's blood is sufficient for her own needs and for those of the fetus. This finding does not conflict with the demonstration by Wilson and previous observers that a considerable nitrogen-storage takes place during pregnancy, but in conjunction with that fact indicates that the nitrogenous food of the mother is promptly assimilated by the two organisms dependent upon it.

Associated with a number of complications of pregnancy normal values for the amino-acids were found. Thus, in a patient with broken cardiac compensation—later restored, and delivery at full term attained successfully—there were 10.7 mg. of amino-acid nitrogen in the blood. Again, in cases of miscarriage, alimentary glycosuria and hydramnios, the values were normal.

When pregnancy was complicated by the presence of an autointoxication, the quantity of amino-acids in the blood was particularly instructive, for the view has long been popular that pre-eclamptic toxæmia and eclampsia are attributable to a derangement of protein metabolism. This view, already discredited by the finding of a normal or slightly increased quantity of non-protein nitrogen in the blood, is also opposed by the fact that the quantity of amino-acid nitrogen present is generally normal. My findings agree with those recently published by Losee and Van Slyke, who failed to demonstrate an increase either in pre-eclamptic toxæmia or in cases in which convulsions were in progress. Occasionally, in my series, values slightly higher than normal were associated with the period of convalescence. Thus, in Case 18 there was a progressive increase in the amino-acid nitrogen during the first and second days after delivery. Recovery also followed in Case 17 which presented the same values on the third day post partum and when the disease was at its height.

While the explanation for the occasional existence of an increased quantity of amino-acids in eclamptics must be purely speculative, it is pertinent to suggest that the dissolution of the corpuscles extravasated in the liver lesion may be responsible. Ordinarily, the destruction of the liver tissue itself is not extensive and would not account for the phenomenon; but at times the hemorrhage into the liver and also into other organs is considerable, so that subsequent autolysis may increase the amino-acids of the blood. If this interpretation is correct, we should expect variable quantities during convalescence, from this disease, for the extent of the hemorrhage is by no means the same in all cases. Whatever the cause of the increase in the amino-acid nitrogen occasionally seen during or after eclampsia, it does not depend upon the kidney lesion. At least this view seems justified by the findings in cases of toxæmia referable to renal insufficiency alone; instances of this kind, Cases 20, 21 and 22, present a normal amount of amino-acid nitrogen.

From the viewpoint of autointoxication two cases, in which the clinical diagnosis was obscure, have a peculiar interest, as they present a great increase in the amino-acid nitrogen. An

outline of their histories is given, for they may be helpful toward the recognition of similar cases in the future. It may prove that an increase in the amino-acids of the blood occurs in a specific form of pregnancy-toxæmia.

In these cases the warning symptoms of eclampsia, including headache, visual disturbance, œdema, and albuminuria were absent, and there was no other reason to suspect that the complication was pre-eclamptic toxæmia. On the contrary the high values (21 mg.) for the amino-acids suggest an autolytic process. It is well known that acute yellow atrophy is often associated with pregnancy and also that autolysis of the liver leads to an increase in the amino-acids of the blood. However, jaundice and a lessened area of liver dullness, typical signs of acute yellow atrophy, were absent. In these circumstances the diagnosis was problematical.

No. 24 (S. J. D.) Primipara; 20 years of age; Wassermann negative. Operation scar in appendix region indicates that the wound was infected. No supervision during pregnancy, but patient states her health has been good. Admitted to hospital in labor. Urine negative for albumin and casts. Breech extraction. Female infant with spina bifida. Though it was 50 cm. long the infant's birth-weight was 2600 grams; the mother's menstrual history indicated she was at term. The infant died on the 3d day after birth. The mother's blood pressure was 150 mm. of Hg. at the time of labor and fell gradually to 120 mm. on the 5th day post partum. She was discharged in excellent condition.

No. 25 (D. R.). Primipara; 18 years of age. The patient is poorly nourished and weak; states she has had headache throughout pregnancy and consulted a physician. No jaundice and no disturbance of vision. Vomiting throughout pregnancy. The urine was negative for albumin and casts but contained a large amount of acetone and diacetic acid. Normal blood pressure. Admitted to hospital with symptoms of impending labor but delivery did not occur until 48 hours later. The first stage of labor caused little complaint and the second stage lasted 55 minutes. During one of the pains the patient fainted. Delivery was spontaneous. The female infant was premature, weighing 2000 grams and measuring 45 cm. in length. At the end of two weeks, weighing 1900 grams, it was taken from the hospital against advice. The mother's convalescence was normal and at no time was there arterial hypertension.

MOTHER AND FETUS AT THE TIME OF BIRTH.

At the conclusion of labor the mother's blood contained a normal quantity of amino-acids, and this remained true even though whiffs of chloroform were administered during delivery. In twelve cases of spontaneous birth at full term the extreme values encountered were 8.1 and 13.9 mg. Similar results were obtained during the period of pregnancy and this fact, in conjunction with the demonstration by Slemons and Morriss that there is no difference between the pregnancy- and labor-values for the total non-protein nitrogen and for the urea, indicates that the transition from the one period to the other is not accompanied by alterations in nitrogenous metabolism. The cause of labor, therefore, must be sought elsewhere. The phenomena which accompany labor and direct suspicion toward nitrogenous metabolism as affording the stimulus in question—a low urinary nitrogen, an abnormal relationship between the various nitrogenous excretory products, and mild albuminuria—must be regarded as secondary. These urinary changes, like

the more pronounced ones in eclampsia, are the results of an etiological factor still unknown.

NORMAL LABOR.

I PARA.

Number.	Source.	Age of mother.	Duration of labor.	Non-protein nitrogen.	Whole blood.				Plasma.	Remarks.
					Amino-acid nitrogen per 100 c. c.	Urea nitrogen per 100 c. c.	Percentage of amino-acid nitrogen.	Percentage of urea nitrogen.		
			hrs.		mg.	mg.	%	%	mg.	
26	Mother.	24	16	10.0	7.3	Whiffs of chloroform.
	Fetus..			13.1	10.8	Normal infant.
27	Mother.	26	5	26.5	13.9	9.8	52.4	36.9	Whiffs of chloroform.
	Fetus..			27.2	15.1	10.7	55.6	39.3	Normal infant.
28	Mother.	25	12	33.5	10.5	31.4	Whiffs of chloroform.
	Fetus..			34.2	15.8	46.1	Normal infant.
29	Mother.	21	8½	8.1	Whiffs of chloroform.
	Fetus..			10.6	Normal infant.

III PARA.

30	Mother.	33	8	10.8	6.7	No anæsthesia.
	Fetus..			10.0	9.2	Normal infant.
31	Mother.	20	13¾	10.1	8.1	Whiffs of chloroform.
	Fetus..			12.9	11.4	Normal infant.
32	Mother.	22	22	10.0	Whiffs of chloroform.
	Fetus..			15.7	Normal infant.

IV PARA.

33	Mother.	36	14	27.7	13.7	13.1	49.4	47.2	Whiffs of chloroform
	Fetus..			27.1	14.8	13.5	54.6	49.8	Normal infant.
34	Mother.	34	4	26.5	11.4	11.6	43.0	44.0	Whiffs of chloroform.
	Fetus..			27.5	12.9	10.0	46.9	36.6	Normal infant.
35	Mother.	25	26	11.2	Whiffs of chloroform.
	Fetus..			12.7	Normal infant.

V PARA.

36	Mother.	23	4½	10.9	10.0	No anæsthesia.
	Fetus..			14.9	11.1	Normal infant.
37	Mother.	23	12½	12.8	Whiffs of chloroform.
	Fetus..			11.3	Normal infant.

OBSTETRICAL OPERATIONS.

38	Mother.	27	15¾	10.7	6.6	Forceps. Chloroform.
	Fetus..	I		13.2	9.1	Normal infant.
39	Mother.	18	21½	9.0	8.2	Forceps. Chloroform.
	Fetus..	I		13.4	11.6	Normal infant.
40	Mother.	30	11.0	Forceps. Chloroform.
	Fetus..	I		10.4	Slight asphyxia.
41	Mother.	30	16	10.8	Forceps. Chloroform.
	Fetus..	VII		15.0	Normal infant.
42	Mother.	35	11.7	Version. Chloroform.
	Fetus..	VII		12.8	Normal infant.
43	Mother.	30	13.0	Cæsarean. Nitr's ox.
	Fetus..	I		13.0	Normal infant.

When delivery has been effected by an operative procedure under deep anæsthesia normal values for the amino-acid nitrogen of the blood are found. Thus, in five cases requiring the surgical degree of chloroform anæsthesia, the average amino-

be regarded as small, though obviously it exaggerates the difference between the maternal and fetal specimens of blood.

In the face of higher fetal values (in approximately 70% of the cases) small as the difference is, mere diffusion cannot be said to explain the passage of amino-acids through the placenta. This problem presents much in common with the problem arising when large amounts of amino-acids are injected into the circulation of an animal. Experimentally, Van Slyke has found that amino-acids pass rapidly into the tissues, and are loosely held there, probably by physical rather than chemical means. An equilibrium is reached when the tissues contain about ten times as much amino-acid nitrogen as the blood does. "The process concerned in the exchange has not been definitely classified and at present we cover our ignorance of its real nature by giving it the general name, *absorption*" (Van Slyke).

Although the equilibrium between maternal and fetal blood is reached when the concentration of amino-acids in the two circulations is more nearly equal than in the case of the blood and tissues in the experiments just quoted, it seems that the placenta like other tissues must possess this same quality of "absorption." On the other hand, the close resemblance between maternal and fetal concentrations is highly significant, indicating an extremely delicate regulatory mechanism for equalizing the amino-acid content of the two circulations per unit of blood volume. The results of this regulation are illustrated by the findings in cases of hyperaminemia (Nos. 24 and 25); in the former identical values (21.6 mg.) were obtained in both organisms, while in the latter 21.4 mg. were found in the maternal and 24.4 mg. in the fetal blood.

The existence of a slightly higher fetal than maternal amino-acid nitrogen in most cases not only suggests the ability of the placenta "to absorb" these substances, but the purpose of this mechanism may be interpreted as protective. When the maternal values are very high, the fetal values duplicate or exceed those in the parent. On the other hand, high fetal values may be associated with normal maternal ones (Cases 28, 32, 41). It seems probable, therefore, that once amino-acids have entered the fetus, it may not be deprived of them, and this provision in a measure insures a supply of material out of which fetal protein is built.

CONCLUSIONS.

1. In normal women the amino-acid nitrogen varied between 8 and 14 mg. per 100 c. c. of blood; and the same range of variations was encountered during pregnancy. In other words, the requirements of the fetus cause no increase of the substances in the maternal blood out of which protein is constructed.

2. Generally, normal values were found in pre-eclamptic toxæmia and eclampsia, though exceptionally an increase in the amino-acids occurred during convalescence.

3. Nephritic toxæmia was accompanied by a normal quantity of amino-acid nitrogen in the blood.

4. An excessive quantity of amino-acids occurred in cases of obscure toxæmia, possibly related to acute yellow atrophy of the liver.

5. During labor normal values were found; at its conclusion the extremes encountered were 8.1 and 13.9 mg.

6. In fetal blood the amino-acid nitrogen varied between 10 and 15.8 mg. per 100 c. c. of blood.

7. The passage of amino-acids from mother to fetus requires the assumption of "absorption" properties on the part of the placenta; for, though the difference between the concentration of amino-acids in the two circulations is small, it is in favor of the fetus in 70% of the cases; and the higher level in that organism prevents the acceptance of simple diffusion as the explanation for the placental exchange.

8. The "absorption" property of the placenta probably protects the fetus against loss of material intended for the construction of protein.

REFERENCES.

Abderhalden: Der Nachweis von freien Aminosäuren im Blute unter normalen Verhältnissen. Ztschr. f. phys. Chemie, 1913, LXXXVIII, 478-483.

Abel, Rowntree and Turner: On the Removal of Diffusible Substances from the Circulating Blood of Living Animals by Dialysis. Jour. Pharmacol. and Exper. Therapeutics, 1913, V, 275-316.

Bang: Untersuchungen über den Reststickstoff des Blutes. Biochem. Ztschr., 1915, LXII, 104-168.

Bock: The Estimation of Amino-Acid Nitrogen in Blood. Jour. Biol. Chem., 1917, XXVIII, 357-368.

Costatino: Der durch Formal titrierbare Aminosäurestickstoff im Blutserum und in den Blutkörperchen von verschiedenen Tieren. Biochem. Ztschr., 1913, LI, 91-96.

Ibid.: Der durch Formal titrierbare Aminosäurestickstoff in den Blutkörperchen und im Serum des Blutes von hungernden und ernährten Tieren. *Ibid.*, 1913, LV, 402-410.

Delaunay: Contribution à l'étude du rôle des acides aminés dans l'organisme animal. Thèse de Bordeaux, 1910.

Fischer: Untersuchungen über Aminosäuren, Polypeptide, und Proteinstoffe. Berlin, 1906.

Folin and Denis: Protein Metabolism from the Standpoint of Blood and Tissue Analysis. Jour. Biol. Chem., 1912, XI, 87-95.

Gorchkoff, Grigorieff et Koutoursky: Contribution à l'étude de l'azote des amino-acides du sang de l'homme dans certaines conditions physiologiques et pathologiques. Compt. rend. Soc. de biol., 1914, LXVII, 454-457.

Greenwald: The Estimation of Non-protein Nitrogen in Blood. Jour. Biol. Chem., 1915, XXI, 61-68.

Gyorgy and Zunz: A Contribution to the Study of the Amino-Acid Content of the Blood. Jour. Biol. Chem., 1915, XXI, 511-537.

Kossel: Quoted by Cohnheim. Chemie der Eiweisskörper. Braunschweig, 1904.

Losee and Van Slyke: The Toxæmias of Pregnancy. Am. Jour. Med. Sc., 1917, CLIII, 94-100.

Mendel: Abnormalities of Growth. Am. Jour. Med. Sciences, 1917, CLIII, 1-20.

Morel et Mouriquand: Comparaison entre le sang du foetus à terme et le sang de la mère au point de vue la répartition naturelle des substances azotées (Urée, amino-acides, etc.). Compt. rend. Soc. de biol., 1913, LXXV, 643-646.

Rosenberg: Bestimmung von freien Aminosäurestickstoff im Blute nach Van Slyke mit salzsäurer Sublimatlösung. Biochem. Ztschr., 1914, LXII, 157-160.

Ross: The Influence of Ether Anæsthesia on Amino-Acids of Blood Serum. Jour. Biol. Chem., 1916, XXVII, 45-50.

Slemons and Morriss: The Non-protein Nitrogen and Urea in

the Maternal and the Fetal Blood at the Time of Birth. Bull. of Johns Hopkins Hospital, 1916, XXVII, 343-350.

Van Slyke: The Quantitative Determination of Aliphatic Amino-Groups. Jour. Biol. Chem., 1912, XII, 275-284.

Idem: The Present Significance of the Amino-Acids in Physiology and Pathology: Harvey Lecture for 1916. Archives of Internal Medicine, 1917, XIX, 56-78.

Van Slyke and Meyer: The Amino-Acid Nitrogen of the Blood. Jour. Biol. Chem., 1912, XII, 339-410.

Idem: The Absorption of Amino-Acids from the Blood by the Tissues. *Ibid.*, 1913, XVI, 197-212.

Wilson: Nitrogen Metabolism during Pregnancy. Bull. Johns Hopkins Hospital, 1916, XXVII, 121-129.

ON THE ETYMOLOGY, POPULAR AND SCIENTIFIC, OF THE TERMS FOR KIDNEY, IN VARIOUS LANGUAGES.*†

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INTRODUCTORY.

The subject of this paper may, on first thought, appear to be more suitable for presentation before a philological rather than a medical assembly. A moment's reflection, however, I venture to say, will suffice to convince that it very appropriately falls within the scope of such a society as this one. The field of interest of medical history is so far-reaching that it overlaps the domains of anthropology, ethnology, and every other branch of biology, among which we certainly must class comparative philology, or the study of the development of speech and its means of communication, or language. An inquiry into the history of some of the simplest terms used in medicine may result in a valuable contribution to the history of the anatomical, physiological, or psychological conceptions of a race or people. That such an inquiry is an interesting discipline, I think, goes without saying. An additional fascination, moreover, attaches itself to it, because for its purposes we are not confined to the limits laid down by what is known as scientific etymology or philology, but may also legitimately draw upon the rich store-house of information classed as folk-lore and popular etymology.

In the present essay, I have endeavored to trace the history of the words for kidney in a number of languages. Such an inquiry was deemed of especial interest because the kidneys have in the last few years been the subject of particular attention and intensive study in this hospital, and because of a number of important discoveries in connection with them which have emanated from this medical school. I am referring in particular to the pioneer work on epinephrin by Prof. Abel¹; to the invention also by him of the process of vividiffusion by means of what has come to be known as an "artificial kidney," of which we have a model here²; and to the introduction of the phenol-sulphone-phthalein test for renal function, also started by Prof. Abel and elaborated by Drs. Rowntree and Gerahty.³ I was further prompted to undertake an investigation of the subject through my keen interest in Semitic philology and Biblical psychology.

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THE ENGLISH "KIDNEYS" AND "REINS."‡

The two English names "Kidneys" and "Reins" illustrate well the composite character of our language, for they take us back to the two most important roots for that organ in the Indo-European languages.

The word "Kidney" consists of two elements "kid" and "ney"; the first of which, according to Professor Bright, must be pronounced unidentified, while the second is probably the same as the German *Niere*. The Middle English form *Kid-nere*, and the Icelandic and old Norse *nyra*, make this relation pretty certain. In Middle English, however, other forms besides *kidnere*—as for instance, *kid-neer*—led to a confusion of the second element of the word *kid-ney*, with *ey* or *eye*, corresponding to the German *Eier*, or testicles. This confusion of the kidneys with testicles, as will be seen later, is met with in many languages.

Although the etymology of the first element *kid* of kidney is uncertain, it has been thought to represent the Anglo-Saxon *cwið* or *cwith*, the Scandinavian *kvíðr* and the Gothic *quithus*, all of which signify stomach or belly. In such a case the meaning of the word kidney would be the *Niere* or the *Eier* of the abdomen, a kind of abdominal tumor. This etymology is, however, not considered correct.

Our other terms for kidneys—*reins*, is readily recognized as the Old French *reins*, which in its turn is derived from the Latin *ren* (pl. *renes*). It is this term in English which is chiefly employed figuratively in the sense of "inward parts, temperament, inner affections or passions." The origin of this expression we shall consider in connection with the Hebrew term for kidney.

THE LATIN "REN" AND ITS DERIVATIVES.

The Latin *ren* (pl. *renes*) is the prototype for the word for kidneys in all the modern Romance languages, and also, as has been just mentioned, of the English *reins*. From it have come the French *reins*, the Italian *rene*, and the Portuguese *rim*; and from its descendant, the late Latin *reniones*, we get the French *rognons* (used of animals only) and the Spanish *riñon*.

The derivation of the word *ren*, according to Prof. K. F. Smith, is altogether uncertain. The old medical writers, however, have some curious notions concerning it. Thus Matthew Timlingio cites Varro as calling *renes* a synonym of *rivuli*,

meaning channels, ducts, or streams. Another curious hypothesis regards *ren* as coming through a metathesis of *n* and *r* from the Greek *νηρόν*, wet or humid. Still other writers consider *ren* to be derived from the Greek *Φρήν* (*diaphragm*, *mind*), from the supposed relation between the kidneys and the mind, but this explanation is obviously a late attempt of the medieval scholars to find a physical basis for their philosophy.

We have another old Latin word for kidneys, namely *nefrones*. This is clearly a transliteration of the Greek *νεφρός*, which we are now going to consider.

THE GREEK "NEPHROS" AND THE GERMAN "NIERE."

Just as the Latin *renes* is the predecessor of the names for kidney in the Romance languages, and of the English *reins*, so is the Greek *νεφρός*, met with so frequently in our present medical nomenclature (*e. g.*, nephritis, nephrolithiasis, epinephrin, etc.), the precursor of the German *Niere* and other Germanic forms, and also probably of the second element of our English *kid-ney*. The relation of *Niere* to *νεφρός* is a very interesting one, and is a good example of the methods employed and results achieved by the modern scientific comparative philologists. Both *νεφρός* and *Niere* come from an original Indo-European posited or hypothetical root "neghros." The g^h of this root, by a well attested relation, appears as φ(ph) in Greek, and thus gives *νεφρός*, from which are derived the Praenestine *nefrones*, and the Lanuvian *nebrundines*. In the Pregermanic or Gothic forms the g^h of the primitive root is softened into an *i*, giving rise to the Gothic *nioro*, the old Norse and Icelandic *nyra*, the old Swedish *niure*, and the modern German *Niere*. (Curtius⁵ 316. Osthoff 1F. N 271 sq. bibl. Brugmann Grdr. I² 588, 613, 634, II², 1, 289, 354, 607, Walde. 1F. XIX, 102.)

That the linguistic relation between the Greek *νεφρός* and the German *Niere* here described is probably a correct one is further substantiated by the fact that both the Greek *νεφρός* and the Old High German *nioro* (masc.) are used in a two-fold sense—sometimes for kidney, and in other cases for *testicle*. Eustathius, for instance, in his Commentary on the Iliad Φ 204 (=p. 1231 ed. Bas.), states this distinctly.

ἔστι δὲ ἐπινεφρίδιος δημὸς ὁ ἐπὶ τοῖς νεφροῖς τοῖς κυρίως, προσεθέμεθα δὲ τὸ κυρίως πρὸς διαστολὴν τῶν μὴ τοιούτων, δοκοῦσι γὰρ ἀστείως καὶ οἱ ὄρχει νεφροὶ κληθῆναι παρὰ τῷ εἰπόντι τό.

This confusion of the kidneys with the testes is found also in other languages. Thus the Old Latin *nebrundines* is used for both *reins*, and *testes*; the Italian *rene*, kidney, means also *testicle*; and some linguists suspect that the Old English phrase "a man of some kidney," where the specific idea expressed by the word comes close to that of virility, might be a survival of the ancient signification of the Greek *νεφρός* and Gothic *nioro*.

The Latin *nebrundines*, it may be well to note, is still preserved in the vulgar German *brunzen*, to micturate.⁶

The comparative philologists have not only succeeded in tracing *Niere* back to *νεφρός*, but have also endeavored to corre-

late *νεφρός* with the Latin *ren*. The process here is a rather intricate one and not very clear, but is of especial interest to the medical student. The Greek word *ἀδὴν* (*ἀδένομος*), meaning gland or tumor, which we find in our medical terms adenitis, adenoids, adenoma, etc., comes from a primitive form ng^hen. From this primitive root or form are derived also the Latin *inguen*, groin, French *aine*, and Old Norse *þekkuen*, meaning tumor or swelling. The form ug^hen is furthermore correlated by comparative philologists on the one hand with the primitive neg^hhron and on the other hand with the Old Irish *āru* (pl. *ārain*), and Gallic *āren*, kidney, which closely resemble the Latin *ren*. It is thus suggested that both the Greek *νεφρός* and Latin *ren* are distantly related to the word *ἀδὴν*, which means a tumor or swelling. (Saussure MSL VI, 53, Brugmann Grdr. I² 391, 408, 593, 634. KV. G. 128, Hirt. Abl. §633. Bezenberger 33, 27, 141.)

The old medical writers were not so well versed in linguistic and phonetic laws, and endeavored to explain the word *νεφρός* on the basis of popular etymology, which meant very often an attempt to correlate the meaning of the word root with their conception of the organ. Though this is not strictly speaking philology, such explanations are of considerable medico-historical interest. Thus, M. Tilingius in 1709, in his Dissertation entitled *Nephrologia Nova et Curiosa*,⁷ regards the word *νεφρός* as consisting of two elements, *νεφ-* and *-pos*, the first of which is related to the word *νέφος*, cloud or mist (*cf.* our word *nephelometer*), whence the verb *νέιφειν*, to snow or rain, whereas the second is related to the word *ρέειν*, to flow (*cf.* *diarrhœa*, *leucorrhœa*, *gonorrhœa*, etc.). The idea suggested is therefore the curious "pneumatistic" conception of the old philosophers, who regarded various spirits or vapors as being condensed in the body and eliminated by the kidneys.⁸

SLAVIC NOMENCLATURE.

Turning our attention from the classical and West European to the East European or Slavic tongues, we meet with a variety of words for kidney, some of which are already familiar, while others are new and peculiar.

The Polish *nyrka* and Bohemian *nerka* are plainly identical with the German *Niere*. Another word for kidney in Polish is *cynadry*. This Prof. Wiener correlates with the German *Geschnader*, and means literally entrails.

Another term commonly designating kidneys in Bohemian is *ledwina* or *ledwinka*. Similarly in Slavonian we find *ledvica*. These three words are all derivatives of the old High German *lenti*, modern German *Lenden*, or loins.

The Russian word for kidney is entirely different from those in other Slavic languages. It is *počka* (pronounced pot-chka) and means a *bud*. The underlying idea is not certain. According to some the word *bud* is used here in the sense of small swelling, and has reference to the shape of the kidney. According to others, the underlying idea may be that of germination and procreation.

The Lithuanian word for kidney is *inskstas*, which means also any hard swelling. The cognate Lettish words for kidney,

inksts, and for the thumb, *inkschkis*, Prof. Prince is inclined to think also express the same idea of tumor or swelling.

In Serbian and Bulgarian the common word for kidney is *bubreg*. This, according to Prof. Prince, is properly from the Turkish *brughrek*, "kidney," and really means something rounded off; an idea akin to the swelling concept.

SANSKRIT.

The Sanskrit tongue which so frequently furnishes the comparative philologist with valuable information, can, according to Prof. Bloomfield, throw very little light on the etymology of the word for kidney in other Indo-European tongues. The Sanskrit word is the *dual vrkkau*, and is related to the old Persian *veredka*. An ultimate analysis of the word is not possible.

ANALYSIS OF THE INDO-EUROPEAN TERMINOLOGY.

Before proceeding to the consideration of some Oriental languages, it may be well to compare the various words for kidneys already studied. It will be noted *firstly* that the meaning of most of the names examined refers to the rotundity or shape of the organ. Thus, both the Greek *νεφρός* and Latin *ren* (which are the forebears of the Romance and Germanic terms) are related to the word *ᾰδών*, and express the idea of tumor or swelling. The Russian *почка*, bud (German, *Knospe*), is also a rounded protuberance or mass. The Lithuanian and Lettish *insktas* express the same idea; and the Bulgarian and Serbian *bubreg* again imply a something rounded off.

Secondly, it is interesting to note the application of the same terms to both the kidneys and the testes. This confusion was obviously due to the close anatomical relationship of the genital and urinary organs, and to the fact that the testes are in many animals to be found situated in the abdominal cavity. Etymologically, of course, the word for kidney, meaning merely a rounded mass or tumor, could be well applied to either testicles or reins.

Thirdly, as a result of this double signification of words, the term kidney came to be employed figuratively to convey the idea of virility or strength. The classical *νεφρός* and the Gothic *nioro* were frequently used in that sense, and as already mentioned, a survival of this ancient usage is probably preserved in our English phrase, "a man of kidney"; or in the expression, "He has no kidney," meaning, "He is a poor specimen of manhood." Compare, again, this passage from George Eliot (*Daniel Deronda*, Vol. II, Ch. 60, p. 334: "There have always been enough of his kidneys, whose piety lies in punishing." Another striking example of this conception is found in old Slavonian, in which the word for kidney is *Mozek*—the literal meaning of which is "little man." In the female a similar relation, it seems, was assumed to exist between the kidneys and the *testes muliebres*, or female testes, *i. e.*, the ovaries.

Lastly, it is well to call attention to the fact that the confusion between the testes and the kidneys was not only from

the anatomical point of view, but also in regard to their physiological function. Preparation or elaboration of the semen was considered to be one of the functions of the kidney in man, and we find this doctrine in medical works as late as the 18th century. Bartholin in his *Anatomia* (Leyden, 1673) cites Olhafius, Sennertus, Wormius, Hofmann, Meibomius, Horstius, Loselius, Eichardius, Sperlinger and others as holding that view, and he himself proceeds then to reconcile it with the phenomena of circulation, recently advanced at that time by Harvey. Horstius (*Opera Medica*, 1661, p. 646) says: "Renum triplex statuitur actio et usus. Primus statuitur in promovendo actu naturalis seminationis." (Of the three uses of the kidneys, the first is in promoting the action of semen.)

Again, in the venerable treatise on kidneys by Tiling (1709), we read:

"Renum usum nobilem non in expurgando solum a sanguine seroso et salso excremento, sed in cocquendo et perficiendo quoque sanguine, itemque potissimum in seminis preparatione ac ejusdem fecundatione consistere." "The noble use of the kidneys is not alone for elimination from the blood of serous excrement and salt, but also in elaborating and perfecting semen and fecundating it." Johan P. Hollardus, in another dissertation, *De Renum Structura et Usu* (Basel, 1705), actually declares that the size of the kidneys is an index of sexual power.

The Russian word for kidney—which means "bud"—seems also to convey this idea. Even Thomas Gibson, in his English "Anatomy of Humane Bodies," London, 1703, p. 131, writes the following: "Some have thought that the kidneys besides the separating of the Serum prepare matter for the seed. . . . This opinion is exploded by the circulation of the blood. Yet, however, though they do not prepare matter for seed, yet by separating the salts and other recrements, they amend the disposition of the blood so that it becomes more capable of being elaborated into seed by the vasa preparantia and testes."

CHINESE AND JAPANESE.¹⁰

Passing to the Oriental languages, we find that the curious and fanciful conceptions just described appear in a more poetical and picturesque garb in Chinese and Japanese, the words for kidney being identical in the two languages. I have received some very interesting information on the subject from Dr. Yates Wang, of the Chinese Legation at Washington. The name *shen tsang* in Chinese (Japanese *zin-zo*), signifies both kidneys and testicles. The Chinese medical philosophers, however, differentiated the functions of the two kidneys. The left one was known as the internal kidney, and had to do with the secretion of urine. The right kidney, on the other hand, was called the gate of life, and was thought to secrete or elaborate semen and to pass it on to the external kidney or testicles.

An ultimate analysis of the word *shen tsang* gives us still more interesting information. The first syllable, *shen*, consists of two elements, the upper one meaning *wisdom*, and the lower meaning *flesh*. The second syllable, *tsang*, means an internal organ for storage of water. The picture language thus conveys

the idea that the kidneys are secreting organs on the one hand, and the seats of wisdom on the other. This conception is peculiarly Oriental, and probably originated from the idea that Wisdom dwells in the innermost recesses and deepest lying organs of the body, such as the kidneys are.

POLYNESIAN AND MALAY.

I have not been able to secure much information concerning the words for kidney and testicles in these languages. Dr. F. R. Blake tells me that the Taglog for kidney is *bato nang kata, wan*, and means "stone of the body," referring as in the European languages to its shape; whereas testicles is *itlog* or ovulum. In Bisaya, the same word is used. In Sulee the word for testicle in *bigi buyang*, *bigi* meaning *seed*.

SEMITIC TERMINOLOGY.

I have purposely reserved the consideration of the Semitic words for kidney for the last, on account of the special interest attaching to them intrinsically, and because of the influence exerted by the Hebrew conception of the kidneys, through the medium of the Bible, upon the use of the word "reins" in English and other modern languages.

The name for kidney is the same in all Semitic languages, with the exception of Sumerian. In Sumerian that organ is called *bir*, which, according to Prof. Haupt, means to tear, lacerate, make incisions, and may have a reference to its indented form. In Hebrew the word for kidney is *kilia*; in Assyrian, *kalitu*; in Arabic, *Kuliatun*; in Syriac, *Kulita*; in Coptic, *Gloote*, and in Aramaic, *kulia*.¹¹ As all these words come from the same root *Kl*, which means to hold or contain, we shall confine ourselves to an analysis of the Hebrew *kilia*.

THE BIBLICAL KELAYOTH.

The Hebrew *kilia* (pl. *kelayoth*), according to Gesenius and most other authorities,¹² comes from the same root (*Kl*), and is really a variant form of the Hebrew word *keli*, a vessel. This being the case, a very curious coincidence immediately suggests itself to the medical man.

In most of the important languages that we may examine, the word for vessel (container, or receptacle), is either alone or with a qualifying adjective "blood," employed to designate *blood-vessels*. Thus we have the English *vessel*, the German *Gefäss*, the French *vaisseau*, the Russian *sosud*, the Latin *vasum*, the Greek *ἄγγος*, and others, all used in both senses. Now, although we find no Hebrew word for blood-vessels in classical (Biblical) literature, in modern Hebrew the expression *keli dam*, "vessel of blood," may quite legitimately be employed in such a sense. The Biblical word for kidneys may therefore be taken literally to signify vessels, or blood-vessels. That, however, is essentially the modern conception of the kidneys—a vascular organ, a "bunch of blood-vessels" or glomeruli, so to say, for the elimination of waste products from the blood. A glance at Prof. Abel's so-called "artificial kidney," which we have exhibited here, and which consists simply of a large number of artificial collodion dialyzing tubes

or "blood-vessels," will make the conception more clear. I am mentioning this curious coincidence, not as an example of scientific philological reasoning, but as an admirable example of how ancient conceptions may sometimes harmonize with modern thought. Moreover, after all such a teleological interpretation of the Biblical *Kilia* is no more forced than the derivation of the Greek *νεφρός* from *ἀδὴν*, for it is very questionable whether *νεφρός* would have ever been traced to *ἀδὴν*, had not the philologists first perceived a similarity in shape between kidney and gland.

It is well to note that the common confusion of kidneys with the testicles and the ambiguous use of the same word to express both so often met by us in the other languages is not found in the Bible. Here we have a distinct term *eshek* (Leviticus XXI, 20) for the latter organ, and in the Talmud the word *bezim* (eggs) are used in the same sense. It is only in Aramaic that the term *kulia* is met with in both senses, and that may possibly be due to foreign influence.¹³

This careful anatomical distinction between the genital (testes and ovaries) and urinary organs (kidneys) met with in the Hebrew literature is undoubtedly due, to some extent at least, to the explicit laws and directions pertaining to the sacrifices. These rites necessitated careful dissection of the animals, and the separation of various organs, among which the kidneys "and the fat that is upon them" occupied an important place.

Though anatomically distinct, the kidneys, however, were correlated with the sexual sphere in a psychological sense. While the head, in Biblical figures of speech, is mentioned as the seat of *thought*,¹⁴ as for instance in Daniel II, 28, IV, 27, etc., the seat of the *will*, and of all higher, nobler and ethical emotions is referred to the heart, "for from it are the issues of life." (Prov. IV, 23.) The kidneys, on the other hand, were believed to be connected with the lower, animal passions, or as some writers describe it, with the *vegetative sphere*.

"Und scheinen somit *kilioth* für das Reich vegetativer Reize und Antriebe dieselbe Stellung inne zu haben, wie das Herz für das Gebiet der höheren Empfindungen und Bestrebungen." (S. R. Hirsch, on Lev. III, 4.)

This figurative use of the word kidneys has passed from the Bible to the modern languages. Thus the meaning of *reins* is given by our dictionaries, besides its primary signification of kidneys, as *temperament, affections, passions*.

Here again the medical man cannot fail to note an interesting coincidence. The relation of the reins to the major emotions, in the light of recent physiological psychology is not merely a metaphoric one. All who are acquainted with the fascinating researches of Cannon and his school on the rôle played by epinephrin in emotive states,¹⁵ will not fail to appreciate the aptness of the Biblical expression—reins, which we must remember always means the *kidneys and the fat that is on them*, i. e., includes the adrenals.

So important was this function considered, that some writers liked to trace a relation between the word *kilia*, kidney, and the root *Kalah*, to long for, to desire passionately.

The Hebrew word *tu-ach*, meaning something covered over, hence, inward parts (Ps. LI, 8; Job XXXVIII, 36) (Vulgate "in visceribus"), has been rendered by some commentators as reins. This interpretation, in connection with the verse in Job "who puts wisdom in the inward parts," led to the erroneous view akin to the Chinese conception, that the kidneys were intimately connected with the seat of wisdom. There is no philological or other basis for this assumption. Wherever the reins are spoken of figuratively as correcting or admonishing, it is always in the ethical sense mentioned above, namely, as controlling our animal or grosser passions. (Cf. Talmud, Berakoth 61, a.)

Finally, I wish to call attention to another interesting coincidence between the Biblical usage of the term reins, and our medical conceptions and associations, and that is the remarkable juxtaposition of the terms heart and kidneys. Out of some 13 passages in which the kidneys are spoken of figuratively in the Old Testament, the word is employed no less than 6 times in apposition to the heart. We find the expressions, "probing heart and reins" (Jer. XI, 20; Ps. VII, 10), "searching heart and reins" (Jer. XVII, 10), "seeing heart and reins" (Jer. XX, 12), "cleansing heart and reins" (Ps. VI, 2). In each case the idea intended to be conveyed is the interdependence of the higher and lower emotions as symbolized by the heart and reins. Just note the literal translation of the Hebrew Ps. LXXIII, 21, "When my heart is oppressed, then am I smitten in my reins." How fitting the simile in these days of cardiopathies and nephropathies, when the two are found to be so closely related as to be impossible of sharp differentiation!

So, as we close, we cannot help but think that the figures of speech and metaphors of the good old Book are up to date, and may be appreciated now as much as in the days of yore—if not, perhaps, a little more!

In conclusion, I take great pleasure in acknowledging with thanks valuable suggestions received from Dr. F. R. Blake, Prof. Paul Haupt, Prof. M. Bloomfield, Prof. J. Bright, Prof. F. K. Smith, Prof. C. W. E. Miller, and Prof. Henry Wood, of this University; from Prof. L. Wiener of Harvard and Prof. J. D. Prince of Columbia; Librarian-in-Chief H. Putnam and Dr. Israel Shapiro, of the Congressional Library; Dr. F. H. Garrison, of the Surgeon-General's Library, and Dr. Yates Wang, of the Chinese Legation, Washington.

REFERENCES.

1. Abel and Macht: Jour. A. M. A., 1911, LVI, 1531, and literature therein.
2. Abel: The Mellon Lecture, Pittsburgh, 1915; and Jour. Pharmacol. and Exp. Therap., 1914, V, 275 and 625.
3. Gerahty and Rowntree: Jour. Pharmacol. and Exp. Therap., 1909, I, 579, and literature therein.
4. Skeat's Etymological Dictionary and Murray's Oxford Dictionary.
5. Boisacq: Dictionnaire Etymologique de la langue grecque (1907-13), and Giles: Manual of Comparative Philology, London, 1901.
6. Grimm's Etymol. Dict.
7. Tiling: Nephrologia nova et Curiosa, Frankf.-on-Main, 1709.
8. Siebeck: Geschichte der Psychologie, Gotha, 1884, II, pp. 128 ff.
9. Hollardus: De Renum Structura et Usu, Basel, 1705.
10. T. Wells Williams: Chinese Dictionary (according to Wu Fang Yuan).
11. Haupt: Am. Jour. of Semitic Lang., 1906, XXII, pp. 205 and 257.
12. Gesenius: Thesaurus.
13. Hyrtl: Arabische u. Hebraische Wörter, i. d. Anat., p. 299.
14. F. C. Delitsch: Biblical Psychology.
15. S. R. Hirsch: Commentary to Pentateuch. Frankfort-on-Main.
16. Cannon, W. B.: Amer. Jour. of Psychology, 1914, XXV, p. 256.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

DECEMBER 4, 1916.

1. Exhibition of Case: DR. J. WHITRIDGE WILLIAMS.

The patient whom you have just seen walk across the amphitheater represents a case of considerable interest in that she sustained a traumatic rupture of the symphysis pubis at the time of labor, and has made a most satisfactory recovery. The history is briefly as follows:

She is 28 years of age. Five years ago she was delivered spontaneously of an eight-pound child. She became pregnant last winter, but was in doubt as to the time of conception. She thought that the last period had begun on December 12, 1915, but was not sure, so that she did not know whether to expect her baby on the 19th of September or a month later. She was registered in the dispensary in the early summer, but nothing abnormal was suspected until she returned on October 20. At that time she had an immensely distended abdomen, and a diagnosis of hydramnios was made. She entered the hospital on October 26, 1916; I saw her the next day and confirmed the diagnosis of excessive hydramnios. Otherwise the examination was not satisfactory, as the

child could not be palpated; all that could be felt was what appeared to be a small head which was freely movable in the lower part of the pendulous abdomen.

In view of the patient's discomfort I told Dr. Davis to rupture the membranes, with the idea that premature labor would set in after the escape of the excess of amniotic fluid. Thinking it a simple matter, Dr. Davis turned the manipulation over to one of the assistants, who after several trials reported that he was unable to find the cervix. Dr. Davis then examined the patient with a similar result. When I was told this at my visit the next morning, I examined the patient by the vagina and could find no trace of a cervix, and upon exposing the vaginal vault by means of a speculum I could not see the external os. I then removed the speculum and examined more carefully with my finger, and eventually felt a little ridge extending transversely across the fornix. On making further pressure, the finger passed into a canal which proved to be that of the cervix which had been distorted by the excessive traction exerted by the distended uterus. The membranes were then ruptured and 5 liters of amniotic fluid escaped. Upon re-examining the patient immediately afterwards, I was surprised to find that the condition had materially changed, and that the cervix readily admitted several fingers.

We then debated whether we should leave the patient alone or complete delivery. I decided in favor of the latter, as the patient was already under anæsthesia and was not doing particularly well. Dilatation of the cervix was readily effected by Harris's manual method, and I started to turn and extract the child. Upon introducing my hand into the uterus I was impressed by the large size of the head, and immediately suspected an unusually large or a hydrocephalic child. I carefully palpated a large child through the abdomen, which was now easy, and, after some little hesitation determined to go ahead with the version and extraction and to puncture the head if necessary. The craniotomy instruments were prepared. Version was comparatively easy, although, as soon as the anterior leg had been delivered, I was impressed by its excessive size. Extraction was effected without difficulty and without the employment of undue force. Indeed, I was rather surprised at the ease with which delivery was completed. The child was unusually large and weighed 5600 grams.

After the birth there was a considerable amount of bleeding, and upon inspecting the external genitalia I found a tear to the right of the urethra which extended up into the vagina. Upon introducing the fingers within it I found that the symphysis pubis had been ruptured, and that the ends of the pubic bones were separated by a space which admitted three fingers. After expression of the placenta, several bleeding vessels were ligated and the tear was repaired with catgut sutures, with the exception of a small opening at its lower end through which a drain was inserted. After the usual dressings had been applied, the hips were encased with a 5-inch strip of adhesive plaster. The patient was considerably shocked after delivery, but made an uneventful convalescence, except for a slight rise of temperature for the first few days after delivery. At the end of three weeks she was out of bed and began to walk, and two weeks later could walk as well as she had before the accident occurred. Three days ago I examined her carefully and found that the vulval tear had healed, that there was no trace of rupture of the symphysis, and that no greater motility existed than in a normal puerperal woman. An X-ray examination showed a slight separation between the ends of the two pubic bones, but only a very little more than usual.

I have demonstrated this patient and her baby for three reasons: firstly, because the accident is a rare one; secondly, on account of the very satisfactory results which followed the simple treatment which I have outlined; thirdly, we had to deal with a prolongation of pregnancy. I have seen three other cases of rupture of the symphysis in my experience. One patient died just after delivery, but the other two were treated just as this patient and recovered satisfactorily. The condition is particularly interesting, as it demonstrates the important difference between rupture of the symphysis and fracture of the pelvis. The latter accident is always a serious one, requires complicated treatment and the patient is usually unable to walk for months, whereas, in the former, the treatment is very simple and the recovery prompt.

2. The Surgical Treatment of Bronchiectasis. DR. SAMUEL ROBINSON, Mayo Clinic, Rochester, Minn.

3. The Mechanism and Clinical Significance of Anaphylactic Skin Reactions. DR. JOHN A. KOLMER, Philadelphia, Pa.

This paper appeared in the May number of the BULLETIN.

DECEMBER 18, 1916.

1. Studies of the Blood Proteins in Infection and Immunity. DR. S. H. HURWITZ, San Francisco, Cal.

2. Is there any Real Analogy between Crown Gall and Cancer? (Abstract). DR. ERWIN SMITH, Washington, D. C.

1. My first acquaintance with this disease began 20 years ago. At that time it was rather prevalent in peach nurseries in California and in Georgia, from which localities my material was

obtained. I worked on the disease about six months without coming to any conclusion as to its cause, but I did not consider the time wholly lost because I reached a definite conclusion that the disease could not be due to insect injuries, to fungi or to slime molds, these being the organisms I had specially in mind. I did not at that time think of bacteria as the cause of the disease, or of the disease as a cancer.

2. Twelve years ago I began on the disease again in conjunction with Dr. C. O. Townsend and Miss Nellie A. Brown. After two years of experimenting we succeeded in isolating the parasite, and published a bulletin from the United States Department of Agriculture on its biology and on the gross appearance and structure of the tumor. Dr. Townsend had then withdrawn from the Department and the whole subject had come into my hands. Even then I thought of it as a cancer (Bull. 213, pp. 161-171).

3. Soon after I discovered the tumor strand and have personally made the other discoveries which seem to connect it with cancer, but have been helped greatly in many arduous labors—inoculations, isolations, preparation of cultures, preparation of sections, etc.—by two assistants who are still working with me, Miss Nellie A. Brown and Miss Lucia McCulloch.

4. Up to this time we have established the following facts concerning this disease:

(a) The bacteria are intracellular. The cells of the host plant are not killed but are stimulated to divide with unusual frequency. The bacteria are not abundant in the cells. They can be cultivated from the tumor tissues by the ordinary methods of the bacteriologists, but cannot be differentially stained within them with any of the aniline stains.

(b) The disease is a hyperplasia.

(c) Secondary tumors are produced.

(d) These secondary tumors are always connected back to the primary tumor by a chain of tumor cells.

(e) The secondary tumors have the structure of the primary tumor; hence the overgrowth is a cancer and not a granuloma.

(f) The common sort of crown gall is developed out of primary or secondary conjunctive tissue. It is, therefore, a sarcoma.

(g) In addition to the proliferating cancer cells, which are quite embryonic, there is a stroma consisting of two types of vessels, which we may liken to the blood-vessels and lymph spaces in animal tissues.

(h) The tumor is sometimes vascularized very abundantly and at other times scantily, according to the greater or less vascularity of the tissue in which it originates.

(i) It is either a hard, slow-growing, long-continued, more or less benign tumor, or a perishable growth quickly invaded by other organisms, and destructive to the plant.

(j) The parasite shows various grades of virulence.

(k) Plants exhibit many degrees of resistance from absolute to slight.

(l) Embryomas. This year it was my good fortune to discover a new type of this tumor in which there are roots, shoots and various embryonic fragments, as indicated in the lantern slides. This type of tumor, to my mind, corresponds strikingly to the most complex animal cancer, that is, to embryomas as they occur in man and animals. [This part of Doctor Smith's paper will appear in full later in the BULLETIN.]

DISCUSSION.

DR. B. E. LIVINGSTON: I should like to ask a question that I think Dr. Smith perhaps may have made clear. I was not quite sure whether this growth went on over long distances after you failed to note your organism. Are we to suppose that the organism gets into the cell, or influences the cell in some way, and that later on the cell can go on for a number of generations plunging out into other tissue in this way without any more of the organism, or do you think the organism goes with it?

DR. ERWIN F. SMITH: Dr. Adami, in one of his letters to me, expressed the idea that while the bacteria might start the primary tumor, the growth could perhaps then go on without them. This I doubt. Growth might go on for a very brief time but not for long because the stimulus would then be exhausted. We have cultivated the organism also from the secondary tumors and once from the tumor strand, so I think we must believe that the organism goes with the tumor. But according to my conception, not one cell in 100 actually has the parasite in it. I conceive cancer in plants to be due to the stimulus exerted by the by-products of the growth of the parasite. These products diffuse out of cells in which they are formed and act on the surrounding tissues.

DR. THAYER: I should like to ask Dr. Smith if he has been able to grow productive growth of this sort by the injection of any products of the bacteria?

DR. ERWIN F. SMITH: I have been able to do this with the products of the organism. These are ammonia, amines, acetic acid, formic acid, etc., that is, substances already shown by Jacques Loeb and others to be among those best adapted to start growth in unfertilized egg cells. These results will be described in a paper which I hope to publish before very long. (See "Mechanism of Tumor Growth in Crown Gall," *Journal of Agricultural Research*, January 29, 1917.)

DR. WINTERNITZ: The ovation Dr. Smith has received expresses our appreciation of his splendid work better than anything I could say. This field of plant pathology, more precisely plant tumors, through Dr. Smith's studies, has been made most attractive and important to those of us especially who are interested in similar problems of human pathology. Unfortunately the latter have not yet reached the happy climax attained in the study of plant tumors.

Tumors of plants are autonomous new growths, they not only do not subserve any useful purpose but ultimately they cause the death of their host. They are, therefore, analogous to human cancer in the broader sense of the latter term. It must be borne in mind, of course, that differentiation and proliferation vary in inverse ratio. The possibility of an abnormal reaction, as the result of an injury, is consequently much greater for the plant with its less highly specialized structure than for the mammal where cell differentiation in some instances attains a stage incompatible with regeneration.

Dr. Smith has produced varied types of tumors by the inoculation of the plant with *Bact. tumefaciens*. Dr. Thayer already has asked whether similar results can be attained with killed cultures, or with chemical products from the bacteria. Dr. Rous, as you know, has succeeded in the production of sarcomata and embryomata of the fowl not only by direct transplantation of portions of similar spontaneous tumors, but also by the injection of cell-free Berkefeld filtrates of emulsions of similar tumors. Comparable results have so far been unattainable with mammalian tumors. It would be interesting indeed if killed cultures or chemical products of the *Bact. tumefaciens* were capable of stimulating neoplasm formation in the plant.

In conclusion, may I ask Dr. Smith in what percentage of spontaneous plant tumors the *Bact. tumefaciens* has been found and whether similar plant tumors can be produced with other organisms or different injurious agents? While, in the last analysis nothing is known concerning the etiology of human cancer, the belief has become more and more general that many different irritants may sooner or later result in tumor formation.

DR. ERWIN F. SMITH: We have plated this organism out of perhaps 30 species of plants belonging to many different families. We do not always get the parasite out, particularly in tumors occurring naturally on the sugar beet. From tumors occurring on this plant naturally we have tried over and over again to get

the parasite and generally have failed. I held back the first department bulletin six weeks to get tumors on beets with the organism plated from sugar beets. On the last plate in that bulletin (No. 213, plate 36), slight overgrowths are shown, which was all we could get for the most active of the colonies tested. Since then we have made perhaps 50 sub-cultures from as many hopeful looking colonies and tried these, but failed absolutely. Yet I believe the beet tumor is due to the crown-gall organism. The same is true, to a lesser degree, of isolations from tumors occurring naturally on other plants (daisy, rose, carnation, etc.). The colonies look all right, but frequently they do not do anything when inoculated into the plant. Out of half a dozen colonies selected from the plate as entirely typical, perhaps only one is virulent. I have thought that possibly inside of the tumor some action of the plant goes on which destroys the virulence of the organism. Some strains of the organism certainly lose virulence on media. One of the most virulent daisy strains we ever had lost all power to produce tumors after about three and one-half years on culture media, and yet appeared to be the same organism.

We now have another daisy strain which we have been carrying about three years and a half (called "resistant daisy" because it was isolated from a tumor which appeared by accident on one of our resistant plants). It was extremely virulent at the start and is still moderately virulent, but evidently is losing out. On the other hand, we have carried on culture media for nine years the strain we plated from the California hop, and it is just as virulent as it ever was. One of my assistants and myself have been working for about four years on a paper dealing with the question of crown-gall species, loss of virulence, resistant hosts, etc. We have got enough data to know that there are several distinct strains of *Bacterium tumefaciens*, e. g., the strains isolated from the daisy produce tumors readily on both hop and daisy, but the hop strain crossed on the daisy will not produce any tumors, and so on. We shall be able to show clearly, I believe, that we are dealing with distinct species. We experiment with all kinds of plants. Cancer experiments on animals have been confined to a very few species. I have often wondered why animal pathologists limited themselves to so few kinds of animals. Perhaps failures to cross-graft cancers to other experimental animals have been due to the fact that you have not had the right kind of animal, just as we have tried to inoculate from the hop to the Paris daisy, or from the daisy to the onion, and have had no positive results.

JANUARY 8, 1917.

Several Brief Reports of Current Work from the Department of Pathology by Members of the Pathological Staff.

H-ion Concentration of Cerebro-Spinal Fluid. (Abstract.) LLOYD D. FELTON.

In work on 76 cerebro-spinal fluids from four groups of patients, normal, senile normal, syphilitic, and epileptic, S. Bayne-Jones, Lloyd D. Felton and R. G. Hussey reported on the H-ion concentration, RpH, refractive index, and Lange's gold reaction as influenced by H-ion concentration. It was found that previous workers had not taken into consideration the unstable CO₂ tension, thus reporting results clearly erroneous. By examining the fluid immediately after withdrawal (as did Bisgaard), the H-ion concentration of the 76 fluids averaged 7.7, there being no characteristic change in any of the diseases studied. The RpH ranges from .6 to .9. Refractive index was found to be between 1.3348 and 1.3351, confirming the work of Babe. Lange's gold reaction was not influenced by the H-ion concentration.

The Oxygen Pressure Necessary for Cellular Activity. (Abstract.) MONTROSE T. BURROWS, M. D.

In an early study the author had noted that the oxygen necessary for cellular activity in a tissue culture comes from the air-

chamber of the hollow ground slide in which the culture is suspended. The cultures were made by placing a small fragment of tissue, 1 mm. in diameter, in a layer of plasma on the surface of a cover-glass. The cover-glass is inverted over a hollow slide so that the medium and tissue hang in the air-chamber. The cover is sealed to the slide with vaseline and paraffine to prevent drying.

In the present study a special type of culture has been constructed. It is so arranged as to allow one to pass into it any gas or combination of gases. The air-chamber of this culture is large, 40 to 60 times that of the ordinary culture in which growth may continue actively for several days. This culture chamber is made from one piece of glass and it can be sealed by fusing. The effect on the growth of the cells of pure oxygen and partial pressure of oxygen have been tested. The partial pressures of oxygen were obtained by diluting pure oxygen with the nitrogen gas. The tissues used have been fragments of heart muscle and skin of chick embryos and foetal chickens. The medium is blood plasma, prepared from the blood of adult chickens. There is a small error in the measurements of the partial pressure of oxygen.

Including this error the results have been considered interesting. The cells grow actively in pure oxygen. The growth, although in some instances possibly slightly more rapid, is not greater in an atmosphere of pure oxygen than that observed in an atmosphere containing 9 or 10 per cent of oxygen. A small growth is seen when the partial pressure of oxygen is as low as 6.6 per cent, 45.6 mm. of mercury, an oxygen pressure not far removed from the known venous oxygen pressure of man. We do not know the venous oxygen pressure of the chicken.

The Interrelation of the Surviving Heart and Pancreas of the Dog in Sugar Metabolism. (Abstract.) ADMONT H. CLARK, M. D.

The experiments indicate that the pancreas when perfused aseptically with Locke's solution containing physiological concentrations of dextrose, does not alter the reducing properties of the perfused solution. The pancreas, however, seems to supply something to the Locke's solution circulating through its arteries which in some way brings about a utilization of sugar by the living heart to an extent that does not occur with the heart alone. This pancreatic substance possesses some of the characteristics of an enzyme. It is inactivated by boiling; it is unstable, rapidly becoming inactive on standing; it acts in small amounts; it causes a great acceleration in the rate of a reaction which otherwise proceeds slowly, and the rate of reaction diminishes as the reaction proceeds. Thus this substance has more of the characteristics of an enzyme than of a stable internal secretion like that of the adrenal glands. The disappearance of sugar was dependent upon the presence of living heart tissue, and it ceased as soon as the perfusate was removed from the heart-pancreas circulation and did not occur at all when a pancreatic perfusate was passed through a non-beating heart. This result indicates that the reaction is not similar to that obtained when muscle and pancreas extracts act on more concentrated solutions of dextrose.

The living heart, in the presence of the pancreatic factor and dextrose, is responsible for two effects: First, a condensation of the sugar to a non-reducing form that yields again a simple sugar on hydrolysis or by simply standing, with a preservative at 37° C. for 24 hours; second, a disappearance of sugar which is probably due to its destruction by hydrolysis or oxidation. After deducting the reducing sugar in the heart-pancreas perfusions which could be recovered by hydrolysis, the amount of sugar which had actually disappeared exceeded that which was used by the heart when perfused with dextrose alone. As to the fate of this portion of the sugar, no definite evidence was obtained.

The question arises as to whether this substance obtained from the perfused pancreas is identical with the hypothetical internal secretion of the pancreas so essential in sugar metabolism.

That there is an internal secretion of the pancreas which can be obtained by this method, and that in some way it accelerates the utilization of sugar by the living heart, seems evident. Though the conclusions are based on the heart and pancreas isolated from the numerous interrelating factors occurring in the body, the evidence suggests at least that the substance or substances obtained by perfusing the pancreas may be concerned in the normal activity of the pancreas upon sugar metabolism.

Anatomical Changes Associated with High Cholesterin Diet. (Abstract.) H. C. SCHMEISSER.

In The John Hopkins Hospital Bulletin, January, 1916, Knox, Wahl and Schmeisser published studies of two cases of Gaucher's disease.

These cases were characterized anatomically by a marked enlargement of the spleen, liver, kidneys, adrenals and to a less degree the lymph glands. Each organ had a characteristic appearance.

The increase in the size of the organ was brought about, as could be seen microscopically, by the presence of a large pale cell with a round or oval, semivesicular or deep-staining nucleus and a granular or finely vacuolated cytoplasm. Similar changes frequently involved the parenchymatous cells.

The all important question was to determine the nature of the material in the cytoplasm of these cells.

Some preliminary microchemical tests and the application of the crossed Nicol's prisms led to the belief that it might be of lipid nature.

Consequently Wahl and Richardson undertook a chemical study and concluded that it was lipid.

In the meanwhile I attempted to produce this disease experimentally.

A number of investigators, and more recently Bailey, have shown that the feeding of lipid-rich substances, as for instance egg-yolk or brain, or pure cholesterin to rabbits produces a deposit of anisotropic fat in various organs.

Making use of this fact, rabbits were fed with large amounts of hog's brain over a long period of time. This resulted in the production of a picture which both grossly and microscopically closely simulates the anatomical findings in the two cases reported as Gaucher's disease.

DISCUSSION.

DR. F. A. EVANS: I had the privilege of studying some of the cases Dr. Mandlebaum admits as Gaucher's disease, together with some slides of Dr. Schmeisser's case, and the cells are certainly different. Whether one is justified in accepting the limitations Dr. Mandlebaum imposes on the diagnosis, Gaucher's disease, is of course open to question, but it is undeniable that the cells in the two cases differ not only in distribution but in morphology. That raises the question as to what were the cells in this case. Are they the same cells as those seen in Dr. Mandlebaum's cases in reaction to different stimuli, or the same cells in different stages of reaction to the same stimulus? In talking this matter over with Dr. Oskar Klotz, he called my attention to the results of some experiments done in his laboratory. In these, cholesterin was injected into rabbits, and a pathological picture obtained apparently the same as that in Dr. Schmeisser's feeding experiments. Some animals were allowed to live after the injections were stopped, and the cells changed their form and reproduced practically the picture of the cells that Dr. Mandlebaum considers typical of Gaucher's disease, the only difference being in the distribution. Did Dr. Schmeisser let any of his animals live after the cholesterin feeding was stopped, and if so, what was the pathological picture?

The Blood-Vessels of the Heart Valves. (Abstract.) DR. S. BAYNE-JONES.

By injecting neutral carmin gelatin at 45°C. into the coronary arteries under a pressure of 160 to 190 mm. Hg., blood-vessels were demonstrated in the arterioventricular and semilunar valves of normal human hearts. The arteries to the mitral and tricuspid valves are distinct branches of the annular divisions of the coronary arteries. These vessels pass down the thicker regions of the valves and ramify in a glomerular-like arrangement along the line of closure of these valves. The chordæ tendineæ receive a few small blood-vessels from the arteries of the papillary muscles. The semilunar valves receive delicate arteries from the vasa vasorum of the aorta and pulmonary arteries and from the blood-vessels of the auricular endocardium.

These studies extend the findings reported by Luschka in 1852 and 1863 and of others who have shown that the normal heart valves are vascularized. The difficulties of the technic are considerable, but when the factors are properly arranged, the blood-vessels of the heart valves can be injected with regularity. The results of these studies give an anatomical basis for the conception that endocarditis may be embolic in origin.

Experimental Nephropathy in the Dog. Lesions Produced by Injection of the Bacillus Bronchisepticus into the Renal Artery. (Abstract.) M. C. WINTERNITZ.

Spontaneous renal lesions are not uncommon in the dog. As a rule they are inconspicuous, but occasionally extensive anatomical changes occur similar, even in their detail, to those found in the human kidney in the progressive, non-suppurative types of nephritis.

The etiology of the disease in the dog is as obscure as it is in man; and it is evident that the two conditions may result from similar causes, and that the great majority of chemical irritants already used for the production of experimental renal lesions can have no more place in the etiology of these spontaneous changes in the dog than they have in the pathology of the human kidney. Promising experimental results have been obtained recently with bacteria as the exciting agent, and this is in accord with the growing impression that microorganisms may be etiologically associated with the more important types of progressive nephropathies in man.

Assuming this impression to be correct, it is probable that the nephropathy of the dog is the result of some acute infectious disease frequent in the species. Accordingly, in the experiments here recorded, the attempt to produce a progressive nephropathy in the dog similar to those of man differs in method from the usual procedures, in that a microorganism, the bacillus bronchisepticus, known to produce spontaneous disease in the species, has been employed.

The organism used for injection corresponded in its microscopical characteristics, staining qualities, cultural reactions and pathogenicity for lower animals to the bacillus bronchisepticus.

About 5 c. c. of either a 36- to 48-hour growth in litmus milk or of an emulsion of a growth, from an agar slant in sterile salt solution, were injected directly into the renal artery. At first both, later only one kidney was injected. The remaining one was subsequently similarly injected, or removed after the acute symptoms following the initial procedure had subsided.

All operations were done under ether anesthesia and with complete surgical asepsis.

The immediate results of this procedure varied markedly. Some of the animals showed definite generalized distemper, with conjunctivitis, nasal discharge, anorexia and loss of weight. Their urine at first contained some blood and showed large amounts of albumin. On the other hand, other dogs showed no signs whatever of general infection, and after the first few days only the slightest traces of albuminuria. The larger number of animals

reacted to the injection definitely, but without the severe generalized infection of the first group. It seems reasonable to explain these results on the ground of variation in susceptibility of the different animals. The severe, overwhelming infections occurred, as a rule, in young dogs, while those showing practically no reaction were old, or had at least attained their full growth. This coincides with the well-known immunity which commonly follows an attack of distemper:

It is possible, therefore, to divide the animals into three groups.

(1) Immune animals that showed only a transient renal lesion and no general reaction.

(2) Animals that died acutely with a fulminating renal lesion and an acute general reaction.

(3) Those which showed a milder renal lesion which progressed after the less severe, general reaction had subsided. In this last group the animals ultimately succumbed to renal insufficiency, provided the uninjected kidney was removed shortly after the acute stage had passed.

JANUARY 22, 1917.

1. Exhibition of Case. DR. T. M. RIVERS.

To appear later in the BULLETIN.

2. Demonstration of an Apparatus for Taking Continuous Blood Pressure Tracings in Man. (Abstract.) A. C. KOLLS.

It is a well-known fact that the pressure in a cuff, inflated to the point at which pulsations in the distal portion of the artery are just obliterated, is equal to the maximum intra-arterial pressure. It is also well known that a sphygmograph which has been connected to another cuff placed below the first one gives an objective method for determining the point at which the pulse is obliterated. The author has made use of these facts and, by automatically forcing air into the upper cuff when the sphygmograph is actuated and allowing air to flow out when the sphygmograph is at rest, has obtained graphic records of the systolic pressure.

Observations are made by placing the two cuffs upon the subject's arm and connecting them so that the lower one may be inflated from the other in order to insure good transmission of the pulsations to the sphygmograph. The communication between the two cuffs is closed when sufficient pressure has been made in the sphygmograph system. The upper cuff is connected with a recording mercury manometer and an electromagnetic device of such design that a valve is opened to a head of pressure (a large bottle which is pumped up at intervals with a bulb) when the circuit is completed and closed when the circuit is broken. Synchronous with the closing off of the head of pressure another valve establishes a communication between the upper cuff and the outside air so that the pressure slowly falls. Thus, when the intra-arterial pressure is higher than the pressure in the upper cuff, pulsations reach the second cuff and actuate the sphygmograph, which breaks a relay circuit and this in turn closes the circuit to the electromagnet, opening the valve between the head of pressure and the cuff. In case the intra-arterial pressure is lower than the pressure in the upper cuff, the sphygmograph is at rest and air slowly escapes from the valve just mentioned. These changes of pressure are recorded on a moving drum by the mercury manometer.

Tracings may be taken for periods exceeding five minutes without marked discomfort to the subject. Observations have been made for 20 minutes without interruption. However, the pressure in the cuffs may be relieved at any time and again brought back to systolic pressure, thereby giving the subject a brief period of relief. Determinations at intervals with the Tycos instrument on the other arm varied only a few millimeters from the calculated pressure as registered on the graphic records.

3. Shock at the Front. DR. W. T. PORTER, Boston, Mass.

THE LAENNEC SOCIETY.

JANUARY 29, 1917.

Chronic Non-Tuberculous Lung Infections. DR. A. H. GARVIN.

Before I take up the subject of my talk, I should like to show you some X-ray pictures of localized lung military tuberculosis, and to call your attention to the sequence of pathological event in these cases. It seems that we are just beginning to have an idea of the sequence of pathologic event that occurs in lungs infected by the tubercle bacillus. There stands out some new work, however, and some old facts which may be profitably reviewed with a new explanation in mind; that an individual or animal infected with the tubercle bacillus for the first time reacts entirely differently from the type of reaction occurring when infected the second time. This change of circumstances is not a generally recognized phenomenon.

It seems to be the truth that general military tuberculosis is almost never diagnosed. The same is more conspicuously true of localized military tuberculosis. The only one perfectly familiar with military tuberculosis is the pathologist. Two recent case histories where in one case the lung was noted to contain but a few râles at the apex, showed an extensive military tuberculosis at autopsy soon afterwards performed, and in another case the lungs were noted to be perfectly free. In a very short period however, the pathological picture of a lung riddled with the ordinary type of crude tubercle was made evident at the autopsy table.

This almost routine failure to make a diagnosis of military tuberculosis in life is conspicuous.

Koch was the first who noted in animal experiment that a second infection with the tubercle bacillus did not progress in the same sequence as the first infection, but tended to remain stationary and to heal. He was followed by other investigators and finally Paul Roemer added much in the detail protocol where animals were infected with varying relation of doses, of culture, of virulence, and of interval between first and second infections, adding much to the present knowledge of the genesis of phthisis as it is met with clinically.

Trudeau was the first in this country to appreciate the relationship of altered reaction and course of disease in animals that received a first and second infection and his work was extended in detail by Doctors Nichol, Allen, Baldwin and later Dr. Krause. Dr. Krause has coordinated particularly the variables that relate to type of first infection, to time interval and to type and size of second infection. This work has been made possible by the possession of old and well-pedigreed strains of bacillus R₁, H₃₇, and B₁.

The important point in this animal experiment work is the development of an acute pulmonic military tuberculosis of a type that can be classified as crude Laennec tubercle type, which is easily recognized by the naked eye and the subsequent complete disappearance of this crude Laennec military tuberculosis. The development of, and the disappearance of, this crude Laennec military tuberculosis is dependent upon the type of first infection and the interval intervening before the second hematogenous infection is given. The military tuberculosis, when the inoculation dose is the second dose, is miraculous both in its development and in its disappearance.

The first clinical bearing of this animal work, of course, is to demonstrate the existence of it in the patient. General military tuberculosis does not adequately illustrate, but it is of interest when the military tuberculosis is localized either to both lungs, to one lung, or more illustrative still when limited to the small anatomical divisions of the lung; namely, a lobe, or part of a lobe. It is still of greater interest if such a localization can be demonstrated and further demonstrated to disappear after occurring.

There is no doubt that this clinically happens. The point of being aware of it when it is taking place is an entirely different matter. If it can happen in the animal, as conclusively as Dr. Krause's experiments illustrate, there is no reason why it should not be expected to happen in the human being. Here also it seems to be true that the diagnosis of localized pulmonic military tuberculosis escapes.

The brief case stories I present illustrate: that localized pulmonic military tuberculosis occurs as follows: in one lung; in one lobe, in part of one lobe; and in one case of one lobe military tuberculosis is illustrated the disappearance of a one lobe localized military tuberculosis.

(X-ray plate demonstration with brief case histories.)

CHRONIC NON-TUBERCULOUS LUNG INFECTION.

A report of nine cases of lung inflammation simulating tuberculosis in clinical story and physical examination, where the diagnosis was first confused with tuberculosis.

Etiology.—A study of the sputum flora, seems to point to the probable cause of the disease by the common secondary sputum organisms, the influenza bacillus being found most frequently, the pneumococcus, streptococcus, and in one case an undetermined Gram negative bacillus.

The time in all cases averaged about four years before the condition was certainly differentiated from tuberculosis. The clinical course simulated tuberculosis quite regularly, in that the patients suffered from varying types of increasing cough and expectoration with occasional periods of loss of weight, chills, night sweats, and, not infrequently, hemorrhages.

Physical examination showed a predominance of lesions in the base of the lung, and in cases where no lesion could be discovered, the examination of the patient in the inverted position after lung drainage for 15 minutes would often reveal a base lesion that otherwise would have been missed. Apex cases require longer time for differential diagnosis than base cases. The differential diagnosis is easiest in base cases because the state of health is usually better than would be expected for the duration of the disease and the extent of lesion, the number of physical signs and the effect of posture on their increase.

The differential diagnosis from bronchiectasis is usually not difficult.

Treatment is posture in one or another type of inverted position to be carried out sufficiently long at each period to thoroughly cleanse the very residual sputum from the respiratory tract. If the treatment is persisted in thoroughly 15 minutes, four times a day, all retension symptoms are relieved and the patient rapidly improves in general health.

Studies were carried out to determine the danger of such secondary organism carriers to neighboring tuberculous patients, with the result that the ordinary cough sputum prophylaxis seems to be sufficient to avoid any carrier danger.

DISCUSSION.

DR. AUSTRIAN: So far as I am aware we have never recognized such a condition here as localized pulmonary military tuberculosis. Probably we have never looked for it. Patients return with symptoms such as Dr. Garvin describes, but we do not take X-ray pictures of their lungs at those times. One has to be prepared to accept absolutely the belief that the X-ray picture in these cases that have been demonstrated is proof that the lesion is tuberculous. Dr. Garvin in some instances did speak definitely of cases that have not been proved to be tuberculous. In one or two instances the tubercle bacillus had not been demonstrated, although the patients were recognized as having a long-standing tuberculosis.

We do see many non-tuberculous lung infections. Some it has not taken four years to diagnose and some it has taken longer.

I can truly say it has taken much more than four years to give relief to them. I recall one patient who has been around the dispensary for seven years, a woman with a typical clinical non-tuberculous infection, who goes through periods of exacerbation and relief and who in addition to cough has large amounts of sputum and some hemoptysis. We have never tried postural treatment with her.

We have been much interested this year in finding at least two cases of infection of the lower lobe with no evidence of disease elsewhere, the chronic non-tuberculous type. Another patient came in this morning, an employe of the hospital, whom we have been watching for four years, whose general condition remains excellent, but who has had persistent cough with large amounts of sputum, and some hemoptysis. I do not recall how many sputum examinations we have made, but we have never found the tubercle bacillus.

We certainly would like to put the patient through treatment with the postural method, but in our out-patient department this may be impracticable; when they get into their homes, I am afraid they would not carry it out. I imagine that with intelligent cooperative patients, under proper conditions of control, one could accomplish considerably more.

From the chronic non-tuberculous lung infections we have isolated various organisms. We have found the streptococcus mucosus in one group, the pneumococcus in another. From a small number we isolated the influenza bacillus in pure culture from the sputum.

At least one of these chronic lung infections has shown a varied flora—on one occasion a pure culture of pneumococcus was grown from the sputum; later a streptococcus mucosus was isolated; again a mixed culture of the two, and at another time the influenza bacillus appeared. Inasmuch as these findings were obtained in the period when vaccine treatment was considered worthy of a therapeutic trial, this patient proved to us a veritable bug-bear.

Dr. Garvin's interesting paper has indicated the value of periodic roentgenoscopic examinations of patients with pulmonary tuberculosis and has outlined a therapeutic procedure that should prove of great efficacy in the management of chronic non-tuberculous infections of the lungs.

DR. GORDON WILSON: These cases of non-tuberculous lung infection have always been of interest to me on account of the absence of the usual toxic symptoms. Although the patients frequently have an evening temperature, there is no loss of strength, and no lassitude. Another point is the somewhat characteristic change in the breath sounds. You do not notice the intensification of the breath sounds and the râles are extremely characteristic. They have a sticky quality that you hear in no other lung condition.

DR. LEUTSCHER: Some years ago everything of a chronic nature was assumed to be tuberculosis. I have been impressed with a number of cases of cough in students following attacks of measles. There was probably some pulmonary infection at the time of the measles, with possibly some lung defect which had persisted ever since. I have followed some of these cases for a number of years now, and the condition has not changed very much. The type of organism varies. I think we found the influenza bacillus mainly in the bronchiectasis cases. Pneumococci and streptococci were found in some of the other cases. As to the type of organism, it seemed there might be one organism at one time and another at another time. Some of our patients have been followed over a number of years, but they have always had the same type of organism, not only so far as smears were concerned but as regards cultural reactions. In some of our cases which were followed as long as seven years the tubercle bacillus could never be found, but there was always a definite organism which could account for the infection.

DR. BOGGS: Some cases in this group are especially interesting to me as in the last few years Doctor Pincoffs and myself have done some work on mycotic infections. We feel we must look to the sanatoria especially for the working out of this field, and that examination of the case that is not clear cut should include the thought that there may be a mycotic infection. Our experience has been that the gross examination of the carefully collected sputum is important. Plating is done between glass plates, and by means of the low power microscope the little nodules are picked out and planted in such material as acid carbohydrate media, to give special encouragement to the fungi and discouragement to other forms of bacterial growth. We have collected quite a number of such mycotic cases. I am not speaking now of the streptothrix type, but of the larger, grosser bodies which grow luxuriantly in carbohydrate media, especially in acid media. Some of these cases have been in no sense chronic, but somewhat acute and rapidly fatal. Others are chronic and are mistaken for tuberculosis.

The types of these organisms that we have had to work with have been very similar. We are not sufficiently sure of our mycology to say what they are exactly, but they belong to groups that are certainly very distinct from the streptothrix. They are more like some of the spores that have been described lately by Meyer of San Francisco. We do feel that there is work to be done in the careful examination of the sputum, of the chronic as well as the acute pulmonary cases, with the specific object of finding out whether or not fungi are present that are not made out under ordinary methods. Many of these forms are quite unrecognizable in stained specimens. One must use cultural methods and the advantage of culture in the way I have indicated must be remembered.

DR. C. A. PENROSE: I would like to mention in connection with these chronic coughs, the prevalence of cough, with râles and bronchitis, in so many cases of gall bladder infection I have seen. Dr. Cullen has asked me to look out for this in a number of these cases, and in about 50 per cent we have found the chronic cough with profuse expectoration and râles. I think the question of a reflex condition should be considered in these chronic cough cases.

DR. KRAUSE: I was greatly interested in Dr. Garvin's pictures showing tuberculosis healed to such an extent that it did not produce a shadow. Several years ago Dr. Soper and I started some experiments with the idea that tuberculosis that went on to degeneration certainly must leave its scar. We reinfected a number of animals by inoculation into the mesenteric veins and killed them in series. Although all the animals that were killed showed a great deal of tuberculosis in the liver during the first three, four or six weeks, we found that at about the seventieth or eightieth day we were dealing with smooth livers. In other words the tuberculosis had disappeared, and even microscopically there was no trace left. I think several of you were here in the spring when I showed some specimens of tuberculous reinfected animals in which the process had gone on to caseation, and after the sixth, seventh or eighth week there was a great deal of normal lung tissue compared to what had been the case a few weeks earlier.

The point Dr. Wilson made is well-worth bearing in mind, particularly for the student who is doing chest work. I have always thought that one of the best general impressions with which to approach a diagnosis of lung disease was that given the same amount of anatomic change, non-tuberculous lung infection is not so likely to give you so marked a picture of constitutional disturbance as active tuberculosis. In non-tuberculous pulmonary disease it is more usual to have the focal symptoms dominate the field; in tuberculosis, the constitutional symptoms are usually in the foreground. It is of course all important to remember that localized pulmonary tuberculosis is almost always apical, whereas chronic non-tuberculous lung disease is generally basal. In arriv-

ing at a diagnosis we should give such general impressions and the law of averages their proper weight. They will put us straight more often than lead us astray.

DR. JANEWAY: We are all indebted not only to Dr. Garvin, but to the various gentlemen who have discussed this paper, for bringing out the various types of lung disease that one never thinks of until his attention has been called to them. One important lesson for all of us is this—that we must not look at sputum as a substance in which we do or do not find tubercle bacilli, but as a means of making an etiological diagnosis. That diagnosis ought to be pressed far beyond the point of whether tuberculosis is or is not present. The great mistake made by most physicians, is that they fail to feel the necessity for making a diagnosis, if they can only exclude tuberculosis.

DR. GARVIN: I do not know how best to answer Dr. Austrian as to whether or not these cases presented as localized pulmonic

miliary tuberculosis are tuberculous. That would need a long discussion; but from the photographs of each, together with knowledge of the clinical histories, I feel sure they are tuberculous; most of them have been sputum positive for brief periods. It is perhaps not absolutely proven in one or two, but the manifestations they show clinically can be only those of tuberculosis.

With the mycotic type of infection I have had no experience at all, perhaps because I have overlooked it.

The point I wish to repeat is the method of treatment of the non-tuberculous cases. I feel that this can be carried out even with dispensary patients if the patients get the point of the treatment and really appreciate it. At first, standing on their heads, as it were, seemed to the patients in this series, ridiculous, but after one or two patients began a remarkable improvement, the performance of posture ceased to be a novelty and patients were perfectly willing to follow directions and improve upon the procedure.

NOTES ON NEW BOOKS.

War Surgery. By EDMOND DELORME, Médecin Inspecteur Général de l'armée. Translated by H. DE MÉRIC. Cloth, \$1.50. (New York: Paul B. Hoeber, 1915.)

An excellent summary of the principles of war surgery embodying the observations of the author and other French surgeons in the present war. The author takes up in the first chapter the types of projectiles, the differences in wounds made by the different varieties of missiles and the various modifications of bullet wounds, which can be explained by differences in velocity, ricochet and turning over of the bullet in the tissues. In every war there has always been a charge by both sides that the opposing forces were using dum-dum or explosive bullets. Similar charges were made by our own surgeons during the Spanish war, and at the onset of the present European war by both sides. The author emphasizes the explosive effects on tissues of short-range shots and ricochets causing the terrible mutilating wounds which surgeons, inexperienced in gun-shot injuries, are liable to attribute to dum-dum and explosive bullets. No attempt is made to give the technique of the various operative procedures, but the general indications for operation are well explained. The book is especially valuable in that suggestions are given for the management of the various injuries from the time the patient has been wounded

on the field until his reception in a permanent base hospital. The types of cases which should be kept as near the front as possible and those which it is permissible to withdraw with safety are emphasized. The general principles of treatment are excellently given. Not enough emphasis is placed on the early and routine injection of antitetanic serum, nor is there any mention of the value of continuous irrigation or of the excellent results obtained by Carrel with Dakin's solution. The chapter on fractures is brief but very valuable, as the management of these cases is taken up from the first dressing. Delorme is an ardent advocate of his own metallic perforated splints which can be easily bent into the proper position for correcting deformities. There is little mention of the great value of extension, especially in fractures of the femur, and the various ingenious means by which extension and coaptation of the fragments can be obtained, while at the same time permitting easy access to the wound. In the treatment of abdominal wounds the author believes that operation should be "considered as only an exceptional method" and he is in favor of the Murphy suprapubic incision with simple drainage of the pelvis. In general Delorme has been impressed by the value of conservative measures as far as possible, save in the treatment of beginning infection where he vigorously emphasizes the importance of wide incision.

NEW PUBLICATIONS.

The following six monographs:

Free Thrombi and Ball-Thrombi in the Heart. By J. H. HEWITT, M. D. 82 pages. Price, \$1.00.

Benzol as a Leucotoxin. By LAURENCE SELLING, M. D. 60 pages. Price, \$1.00.

Primary Carcinoma of the Liver. By M. C. WINTERNITZ, M. D. 42 pages. Price, 75 cents.

The Statistical Experience Data of The Johns Hopkins Hospital, Baltimore, Md., 1892-1911. By FREDERICK L. HOFFMAN, LL.D., F.S.S. 161 pages. Price, \$2.00.

The Origin and Development of the Lymphatic System. By FLORENCE R. SABIN. 94 pages. Price, \$2.00.

The Nuclei Tuberis Laterales and the So-called Ganglion Opticum Basale. By EDWARD F. MALONE, M. D. Price, \$1.50.

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UNDERGRADUATE INSTRUCTION IN TUBERCULOSIS.¹

By ALLEN K. KRAUSE.

(From the Kenneth Dows Fund for the Study of Tuberculosis, of the Medical Clinic of The Johns Hopkins Hospital.)

I should like to make a thorough investigation of undergraduate instruction in tuberculosis, because I think the subject deserves it and demands it; but the limits of this paper forbid this. I shall therefore confine myself to the exposition of a few matters as I see them, imperfectly perhaps, incompletely and with no gray hairs of experience behind me; yet, withal, with honesty I trust and a consuming desire to help and do my share.

Tuberculosis teaching in our medical schools is an unsolved problem. It demands attention and more active consideration than the passing of resolutions in committee meetings. I believe its solution to be the most pressing one before us to-day. Have you ever stopped for a moment to consider what it would mean if every year every one of our several thousand graduates in medicine left school with some interest in tuberculosis, with some idea of how to make a diagnosis, with some judgment of what to do with the patient once he labelled him? What do

you think would be the situation if fifty years from now every practising physician appreciated the relations between infection and disease, the relative value of signs and symptoms, the importance of the practice of conservative medicine on those who reacted tuberculously but were not tuberculously ill—the pregnant woman, the man with a common cold, the child with measles, the patient about to undergo a serious surgical operation? What, if in thinking of tuberculosis every physician's instinct immediately sensed curability of infection, arrest of disease and recrudescence of clinical arrest? What, if his social sense at once responded to the fact that in nine cases out of ten tuberculosis bankrupts, that the disease leaves *young* widows with *young* children, that its victims spread infection for years as against the months of the syphilitic, that syphilis hampers while tuberculosis disables, that cancer meets the man after he has arrived, whereas tuberculosis strikes him down as he is beginning the race? What, if throughout the land we had all these men, these foci, who have real knowledge and therefore real interest, who have their fortunated patients and their honest derelicts, in whom the rich confide and on whom the poor de-

¹ Read before the Clinical Section of the Thirteenth Annual Meeting of the National Association for the Study and Prevention of Tuberculosis, Cincinnati, Ohio, May 11, 1917.

pend, who could so well arouse Dives to come to the aid of Lazarus? All this is common knowledge among specialists. Can it not be made available to our students?

It can. The material to work on is at hand in every medical school where the student can get a glimpse at the sick and the dead, at the autopsy table and the microscope. Everywhere there is the person who harbors tubercle yet is not ill with tuberculosis, the man who runs the gamut of physical examination before a diagnosis of tuberculosis can be accepted or ruled out, the consumptive who makes his own diagnosis. Everywhere there is the patient whose management you must arrange, the man who once had tuberculosis but who is now well rid of it, the "cure" who returns, again broken down and discouraged. In every clinic, no matter how primitive, you will see the face tighten and you will listen to the despairing tones as you give your opinion, to the story of the lost livelihood, of the dependent relatives, of the black economic outlook. No medical school can say that it is too poor to teach tuberculosis. It can no more escape the ubiquity of the tubercle bacillus than can the cabin in the city alley.

Now it has been said that even although the facilities to teach tuberculosis are given, the medical student has no interest in the subject and cannot be interested. This I do not believe, and I cannot help thinking that the affirmation too often shifts the burden of reproach from the teacher, where it belongs, to the student. It cannot be denied that the American medical student is awake to everything that is interesting or is presented in an interesting manner. Nor can it be gainsaid that nothing so lends itself to lively and living exposition as tuberculosis. Of course, a good deal depends on what we mean by tuberculosis. A drab, relentless routine of percussion of pale and sickly patients and of sentence to the same grind of treatment will no doubt discourage many a student and leave him cold. But tuberculosis as a subject for study, as a subject for teaching—what more can any man want? Tell me anything that offers so great and so unique an opportunity to both student and teacher as tuberculosis, which ever since men began to live together has entered so largely, so intimately, so dreadfully into their lives. Tuberculosis: a disease of every part of the earth, of every historical era and of every race; a disease of infancy, of adolescence and of old age; a disease that exerts its effects on every organ and tissue of the body, that may be isolated or may be wide-spread or may take on almost every conceivable combination; that may come like the lightning stroke or more insidiously than the advance of age itself; that may kill in a week or drag out its career through a normal life span, a lazy career perhaps, perhaps a checkered one, but never a colorless one; a disease, too, whose active cause is known and is scarcely less interesting or less versatile than the effects it produces—how wonderful is this trinity of bacilli, human, bovine, avian, so like and yet so unlike; how wonderful their less combative cousins, the saprophytic acid-fasts! And if we would go on and enumerate other attributes—the universality of infection, the indifference of the germ to the portal of entry available, its armor against the body's weapons, its habits of hibernation and rejuvenescence, its triumphs as we

read the roll of victims—and there are both quantity and quality there—and as we proclaim it captain of the hosts of crushed ambition and of death; when we consider the imitations of almost every other malady that it paints and how it leads us through the realms of all medicine if we would tag it; when, in addition, we consider how often and how much it leans on other diseases and on the habits and constitution of man to exert its effects, then we would ask, "What then would a man rather study, what rather teach than tuberculosis?" Laennec and Louis and Virchow and Cohnheim and Austin Flint and Trudeau are inspiring enough and good enough company for any man.

In planning tuberculosis teaching there will probably never be complete agreement of opinion as to the curriculum and the personnel of the teaching staff. It is only natural that the dispensary, the wards of the general hospital, the laboratory or the sanatorium, in turn, should be emphasized by men whose interests and activities lie in any particular field. Tuberculosis itself is breaking up into a number of specialties, and the men who single-handed can present the subject in an adequate and well-rounded manner are very few indeed. There are those who look upon the diagnosis of early disease as the heart of our present problem. There are others who believe systematic segregation of the open case to be the essential point of attack. There are some who declare frankly that there can be no solution until the discovery of some therapeutic agent that will cure practically every variety of case. There are not a few who are convinced that at bottom the problem is an extra-medical one, that its roots are embedded and flourish in the bed-rock and top-soil of our present-day civilization which is the flower of ages of evolution and social conventions, and that nothing less than a slow, laborious and complete revolution or development of social habits and customs can effect a radical change in the situation. In our dilemma it is likely that, as always, Truth is many-sided, and that no one man or group of men has a monopoly of wisdom, and that if we are to impart our available information to our students we must correlate in a practical way the abilities and efforts of a number of men working in particular fields.

This, you will say, is nothing else than a repetition of a general medical course applied to a special subject and involves more time than can be devoted by the medical undergraduate. It is indeed a wheel within a wheel, and for a few minutes I wish to detail how such a plan is feasible and practical. And understand, that since I believe that tuberculosis will play a larger part in a practitioner's professional life than any other disease, I do not think that we need be backward in asking our medical faculties for all the time that they can allot to the subject.

As matters stand now, the student, even though no formal course in tuberculosis is offered, really sees a good deal of tuberculosis and hears a good deal about it during his four years in the medical school. During his course in pathology and in every general and special clinic he sees a variety of tuberculous conditions and hears their nature, their diagnosis and their treatment discussed. But as a rule they are here pre-

sented as incidents, as isolated and individual affections, and except by the unusual man their broader aspects, their relations and their points of contact and contrast as regards tuberculosis at various stages, locations, time of infection, immediate cause of disease, etc., are scarcely touched upon. In the general and special clinic, tuberculosis is taken up in an incidental and not a systematic manner. It is an occurrence that flashes across every day's routine and is very properly handled as such. The result is that the student picks up some very valuable points of diagnosis and, if he is receptive, carries away the accepted method of treatment. But his idea of tuberculosis is not enlarged and he may see hundreds of cases without getting the first fundamental conception of the life history of the individual case (not patient) of tuberculosis, the conception that in almost every instance clinical tuberculosis is the fruition of a seed implanted in the obscure past, nourished, blighted and again nourished by all the vital incidents that have entered into the physical life of the individual.

It is of the utmost importance, however, that the internist, the surgeon, the laryngologist, the pediatrician, the orthopedist, the urologist, continues to teach tuberculosis as he is doing at present. But it is very necessary that we supplement this instruction by some systematic and correlated course in tuberculosis: a course that is all tuberculosis, that selects its material from the other fields of medicine and weaves it all into an orderly, consistent fabric, the warp and woof of which are tuberculosis, the technical threads of which are refined and polished, and the cloth ready to be made into a fit garment when the occasion arises.

Such a course should aim to interpret and correlate systematically all that the student has seen or is likely to see in his contact with all kinds of tuberculous patients. Besides this, it must be based on a clear idea of what the requirements of the situation are, what is most worth while to the student and what will most contribute to the advancement of the anti-tuberculosis movement. It must not spend itself in an aimless recital of physical signs and symptoms and of the management of the patient. It must have a proper sense of proportion and proceed along lines that take into account the relative weight and emphasis to be given to the various phases of what has come to be known as the tuberculosis problem.

Fully aware that I at once lay myself open to contradiction and disagreement, I would enumerate in the order of their relative importance the things that should be taught the student, as follows: First, the importance of *not* making a diagnosis of tuberculosis; second, some rational idea of what to do with the patient once he has been called tuberculous; third, the relapsing nature of the malady; fourth, some conception of the relative value of signs and symptoms in evaluating the individual case and a firm and lasting impression that no disease is quite so notorious as tuberculosis in disharmony of anatomic change, physical signs and symptoms; fifth, the fact that every tuberculous patient must be handled strictly as a personal entity and his course directed only after full and complete knowledge of his family, social and economic conditions; sixth, the technique of making a diagnosis. You

will at once see that several of these phases cannot be sharply cut off one from the other and that they overlap. I assume that the student has had an elementary course in general pathology and that he has had bred into him the habit of applying his pathological senses to all clinical manifestations that he may encounter, although here also I would take up tuberculosis in its special manifestations. If you will refer to the list that I have just outlined, I believe that you will agree that in general its arrangement corresponds with the difficulty and length of time it took us to acquire our own experience of any particular aspect.

To put the matter briefly and sharply, our teaching problem is to give our students the broadest and most practical view of tuberculosis in the shortest possible time and with the least interference with his other courses. He must begin clinical acquaintance with the disease in his third year. He should receive instruction in it in connection with all his other clinical courses, for this will constantly breed into him the instinct of the universality and the innumerable ramifications of tuberculosis. He should in addition be given the opportunity to study tuberculosis in a formal and well-formulated manner and be taught by men whose experience has shown them what to present and how to present it. The material to work on is everywhere abundant, but in too many places the necessary organization and facilities are lacking.

The necessary tools are a tuberculosis dispensary, an adequate laboratory (though it is remarkable how much can be accomplished with a thermostat, a centrifuge and a modicum of glassware) and an able and enthusiastic teaching force. A most helpful adjuvant is a tuberculosis ward. I do not, however, consider the ward as necessary to the undergraduate student, though it may be very valuable to the teacher and advanced student. The first and main impression that the beginning student of tuberculosis should get is the right impression, and to get the right impression of tuberculosis one must become familiar with it in its environment. I would therefore recommend that the student do a certain amount of out-patient work; in fact, I consider this almost necessary for a proper appreciation of the disease. I cannot see how the undergraduate will pick up in the tuberculosis ward anything of prime importance that he cannot just as well get in the dispensary or in the home. As a matter of fact, too much acquaintance with ward patients at the beginning may give him the wrong impression, for here he would work only with diagnosed patients; and the consumptive lying in a clean bed in a bright room and receiving the best of care is not the usual picture of the disease.

In the dispensary, of course, the student will first meet the man who walks in because he isn't feeling just as he should. He will form his acquaintance and listen to his story and record it. He will be taught the great importance of a medical and social history, particularly in such a patient. He will make a physical examination of the man and record what he has found. In company with the dispensary physician and teacher he will study the case. He will be intensively instructed in the technique and mechanics of physical diagnosis.

He will take the patient's sputum and other specimens to the laboratory and examine these himself. He will look into the patient's home life and occupation or will have it reported to him by the dispensary nurse. He will discuss the patient's management with the dispensary physician, and here we shall leave the individual student for a while.

To get the best results, results that are best for the student, teacher and patient, only a few students, three or four, should work in the ordinary dispensary at a time. But matters should be so arranged that every student spends at least 32 hours, that is, two hours a day twice a week for eight weeks, in the dispensary. In this time he can fall in with a good variety of patients and can acquire some slight facility in percussion and auscultation of the chest. He should at least have acquired some sense of his own limitations. And this leads me to the matter of diagnosis in general and of early diagnosis in particular.

I won't say that the majority, but I will say that many cases of pulmonary tuberculosis need no physical examination for diagnosis. As a rule, the patient's associates at home can diagnose what we call consumption. In a great many other cases sputum examination (and it is not practised enough or often until days, and perhaps weeks, have been spent in elaborate chest examinations) will proclaim the condition. But it is remarkable how much scolding we physicians have had from extremists of the early diagnosis school. We would almost gather from some brochures that, if he had been alert enough and keen enough and not too ignorant, every physician might have saved every consumptive's life had he picked up the disease at its first flicker. I realize that the purpose of these propagandists is most worthy, though I do not believe that early diagnosis deserves the importance in the tuberculosis firmament that some would give it. Trying my best to know and understand conditions that exist, I consider it only a minor arm of the service in our battle. All this when I realize that in so many instances patients with insidious tuberculosis first consult the physician only after the malady is well expressed and that in so many others the disease begins abruptly and acutely in a way that cannot be considered incipient in point of extent of lesion and symptoms.

Now just because of this warped and narrow vision of tuberculosis it has come about that in his course the student only too often has got the idea that the detection of the ultimate râle is about all there is to tuberculosis, and he promptly proceeds to polish off his technique so that he can compete in the game. He has also heard of milk and eggs, and equipped with the knowledge that persistent, localized râles after coughing so often mean tuberculosis, and with a hazy belief in the potency of milk and eggs, and profoundly ignorant that there are things like symptoms and medical history and individual habits to be considered, he goes out to snare his tuberculous patient. This is the situation that I protest and I do it with the fullest respect for early diagnosis in its place and believe absolutely that training and proficiency in physical examination is the very corner-stone of medical diagnosis. But I sometimes wonder whether all the tragedies resulting from failure

to diagnose early have not been more than atoned for by the tragedies of a false diagnosis of tuberculosis. Therefore, the first deep tract that I would lay down in the student's brain is one that ever warns him never to make a diagnosis of pulmonary tuberculosis unless he can prove it. He may have his opinion and he may have his patient undergo what is substantially treatment for tuberculosis, but he should not voice a flat opinion to the patient nor should he send him to a tuberculosis resort.

All this analysis of history and signs and symptoms can be taken up in the dispensary with the student, who should not leave the medical school without acquiring a sense of proportion that is well balanced and which he can put into practice. It is in the dispensary that the student must get method and data and some point of view. But in addition to this he must have his point of view clarified, broadened and well grounded.

This enlargement and strengthening of vision is to be done by clinics and by lectures. In eight or nine clinics and ten or a dozen lectures a great deal can be accomplished. The clinics should be well ordered and proceed from one to the other in a developmental manner. Not too much emphasis should be paid to the eliciting of signs, as these can be best worked over in the dispensary. But an effort should be made to present as many people as possible to the student and in an interesting manner to recite the past and present history of these people. Beginning with a display of children whose skins do not react to tuberculin, we can then show some that do but who have never had clinical tuberculosis. We can then go on to those who are now in the best of health but who have a history of one or more attacks behind them. We can exhibit children who are for the time being ill with tuberculosis. We can meanwhile take the opportunity to discuss contact, methods of infection, latency, types of disease, and in general contrast the situation in the child with that in the adult.

Our next clinics would take up the adult. Pulmonary disease is now the type. We may present healthy men who have put severe disease behind them. We show acute tuberculosis and chronic tuberculosis and the combination of these. We show the disease that began with hæmoptysis, that with onset with cough and expectoration or with pain or with transient, daily lassitude. We discuss the significance of symptoms, the technique of laboratory diagnosis, the balancing of history and signs and symptoms, the amelioration of symptoms, the relapse after arrest, the method of treatment and the ultimate prognosis. All these nine clinics should be so arranged that, beginning at the first clinic with infection without clinical disease in the child, we proceed step by step to a demonstration of prognosis in the adult and prophylaxis in the last clinic. And throughout all of them an effort should be made to bring into harmony what the student has seen in the other services of the hospital and to give each manifestation its proper place.

The student is now ready to take up tuberculosis in its broadest aspects. Following the clinics he should be given a course of about a dozen lectures that would deal with such matters as the pathology of tuberculosis, the place of the disease in the history of medicine, the history and attributes of

the tubercle bacillus, the factors that influence infection, the development and effects of infection, the conversion of infection into disease, the spread and arrest of disease, the nature and effects of tuberculin, hypersensitiveness and immunity, therapy, prognosis, prophylaxis and the social side of tuberculosis. The aim of such lectures should be not so much to stress the obvious as to guide and arouse the student and to prepare him to handle his future acquaintance with tuberculosis in a rational and logical manner.

Now all of this dispensary, clinic and lecture instruction can be given during the third year with a maximum of about 50 hours of attendance. The dispensary work is mainly to develop method; the clinics and lectures are largely orienting and interpretative. The student goes to his work in the other services of the medical school immeasurably better prepared to appreciate all the cases of tuberculous disease that he may encounter. Additional instruction that might be arranged would be joint clinics held by the teacher of tuberculosis and the pediatrician, the orthopedist, the laryngologist, the ophthalmologist, the roentgenologist or the surgeon. That such a course in tuberculosis is not an unattainable ideal is evidenced by the fact that it is to-day being carried out in most of its details in one of our medical schools.

Besides the required work that has been outlined above, other opportunities should be offered those students who have the time and inclination to make use of them. In the laboratory there should always be a few desks available where the selected fourth-year student can begin the study of the special bacteriology, serology and clinical microscopy of tuberculosis and can take up the simpler methods of animal experimentation. Such elective courses are, however, hardly worth while unless the student's course is so arranged that he can devote three or four consecutive hours a day two or three times a week over a period of one-third of the scholastic year. Unless the laboratory facilities are very unusual, not more than two or three students a year should be allowed to elect such work.

The out-patient work of the dispensary is capable of great development and should be utilized to better advantage. It is of the utmost importance that we devise some method whereby the student can get a consecutive view of the progress of a case of tuberculosis. In no other way will he have quite so good an opportunity to become familiar with and gain an appreciation of the ups and downs of the average patient. If he can follow intimately one or several cases over a period of months or a year or two, he will gain a valuable and lasting impression of the pendulum-like progress and decline of the ordinary tuberculous patient, and under proper guidance may learn lessons that otherwise might take him years to acquire in practice. We have, therefore, called for volunteers from our third-year students, who for the remainder of their medical course pledge themselves to visit dispensary and discharged sanatorium patients. We plan to have them undertake toward these patients the shadow or even the reality of the family physician. They will be under the supervision and guidance of the dispensary physicians and the visiting nurse. We aim to emphasize the human relation between attendant and patient. We

put the matter to the patient frankly; we want to help him, we are not planning to do any detective work; we want to prevent relapse, we are trying to give him a better chance of ultimate and lasting recovery from his disease; we want him to make a friend and a confidant of our student. The student on his side now has a rare opportunity to learn a great deal about real tuberculosis and, as he frequents the home of the dispensary patient, he also begins to learn something about the ultimate problem of the conquest of tuberculosis, something that makes a lasting impression and which will give him no small impetus when he begins his medical practice. We for our part can keep better track of some of our dispensary patients and can do a good deal of social service work at a minimum of expense. Although the details of this plan have not been worked out, I am confident that it is workable and that it is capable of great development. I am also sure that there will be no dearth of volunteers from the student body.

In the dispensary work the effort should be made to give the student as intensive a training in physical diagnosis as the time and the facilities allow. But it is obvious that even under the best conditions the student cannot become a finished examiner with 32 hours of work. As in everything else, the only way to learn physical examination is to practise it, and it is highly desirable that some arrangement be made whereby the student who desires to go further into tuberculosis will have the chance to work among large numbers of patients. In this connection a ward in a hospital would be valuable, for here several advanced undergraduates might always have the opportunity to perfect themselves in physical diagnosis. But it seems to me that a better plan would be to enlist the coöperation of the tuberculosis sanatoria.

It has been frequently stated that the medical staffs of our sanatoria are undermanned, and that it is difficult to interest in this work men who have not had tuberculosis themselves. Why would it not be a good plan for the sanatoria to use our third and fourth year students as clinical clerks or internes during the summer vacations? For three or four months the student would be assisting in the institutional work. He would make frequent examinations of a great many patients of various types. He could do part of the clinical laboratory work and sometimes carry on a small piece of original research. He would relieve the permanent resident staff of a great deal of routine work and thus give the residents more time for study and investigation. He would himself be gradually absorbing a point of view of tuberculosis that he could get in no other way and learn much about the systematic and disciplinary treatment of the tuberculous. At the same time the ambitious student, worn perhaps after a year's hard work in the medical school, would be supplementing his course in surroundings that would be attractive and would physically benefit him more than the same length of time spent in the hot and dusty city. The sanatorium is bound to get a good deal from the student, but it must also give something in return. It should provide full maintenance for the student. It must not make an orderly out of him, nor simply fill his day's routine with mere drudgery that the residents are glad to be rid of. As a rule, the student

will come ready to work and very anxious to learn. The sanatorium must take enough personal interest in him to see to it that he is taught. This plan is already being tried by Dr. D. A. Stewart of Manitoba, and I believe it capable of great development. To be most effective it should be used as advanced training, that is, for those students who have already had some clinical experience and formal instruction in tuberculosis. It should be for the man who elects it, the man who shows a voluntary interest in the subject.

This sketch of a course of instruction in tuberculosis has been evolved with but one idea in view. It aims to be practical, to make use of conditions such as exist at most medical centers. If any particular clinic is blessed with an ideal equipment and facilities, then that is another matter and we would outline what might perhaps be an ideal course. But I think that it is a great mistake to wait for the arrival of big things before attempting to do anything and in an organized and system-

atic manner to make use of what is at hand. The use of dispensary patients, a small clinical laboratory, coöperation with other services and with tuberculosis sanatoria, and ambitious and interested teachers are I believe attainable anywhere, and we of the National Association should make it our business to convince our general medical faculties of this fact.

We too must use our best efforts to arouse those whose special interests lie in other fields of medicine to the importance of the study of tuberculosis. We must show them that we believe that tuberculosis is vastly more than a particular affection of the lungs. We must do our work so that no orthopedist, no pediatrician, no urologist can afford to neglect it. We can learn much from them if we indicate to them research problems in their particular branches on which they can profitably work. But we should go about this, interested not too obtrusively in the National Association as such, but with our energies whole heartedly given to tuberculosis.

THE MINERAL METABOLISM OF EXPERIMENTAL SCURVY OF THE MONKEY.

By C. P. HOWARD, M. D., and T. INGVALDSEN, M. Sc.,

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In 1912 one of us published with L. Baumann¹ the mineral metabolism of a case of scurvy in an adult male. No further human cases having appeared in our clinic we next turned our attention to the study of experimental scurvy in the guinea-pig.² Realizing that the higher anthropoid apes and monkeys were more suitable to our purposes, we have spent the last year or two in studying the mineral metabolism of the monkey (*Macacus rhesus*). Strange as it may seem the earliest use of the monkey for this purpose was in 1900, when Jackson and Harley³ fed one group with rice, corn and small amounts of fresh meat without the appearance of scurvy; a second group was fed with similar amounts of putrid meat without vegetables and a third group with similar putrid meat and vegetables. In both the second and third groups scorbutic symptoms were found. The authors concluded from this that the putrid state of the meat and not the insufficient quantity of the food was responsible for scurvy.

Twelve years later Carl Hart reported in a series of papers^{4, 5, 6, 7} and finally in monograph form⁸ anatomical studies of scurvy produced in monkeys. In five young monkeys fed on condensed milk and water for periods varying from two to four months there appeared a hæmorrhagic condition of the gums, loosening of the molar teeth, exophthalmos from intra-orbital hæmorrhages, œdema of the eyelids, subperiosteal hæmorrhages of the skull, a bloody diarrhœa, swelling of the epiphyses of the long bones and fractures of both humerus and femur. In addition, the radiograms showed the white line described by Fraenkel. In from one to two months from the onset of the symptoms death occurred associated with loss of weight, apathy and extreme sensitiveness to handling resulting in the "jumping-jack" phenomenon described

by Heubner in the child. At autopsy Hart noted (1) hæmorrhages into the soft tissues and beneath the periosteum and into the marrow of all the bones, (2) degeneration of the marrow of the subchondral-diaphyseal border and (3) rarefaction of the entire bone substance and abolition of the endochondral new bone formation. This resulted in the production of the "Gerüstmark" or the "framework marrow" of Schödel and Nauwerck, namely, a marrow consisting of mucoid or fibrous tissue, poor in blood-vessels. There was a persistence of the calcium at the endochondral ossification zone. Lastly there appeared an area of débris—the "Truemerfeld Zone" of Fraenkel, which is responsible for the white line in the skiagram. One monkey, however, showed signs of typical rickets which Hart explains by suggesting a common cause for both rickets and scurvy, some individual predisposition determining which disease will develop. Four of the 10 monkeys developed neither scurvy nor rickets. One will readily recognize in this description the characteristic symptoms and post-mortem changes seen in the adult and in the infantile scurvy of man.

Hart's work was confirmed in this country in 1913 by F. R. Talbot, W. J. Dodd and H. O. Peterson.⁹ One monkey showed typical clinical signs and a positive radiogram, but at autopsy the bones did not show any scurvy or rickets. Yet there can be no doubt that this animal was suffering from scurvy, since at autopsy there were other evidences of the disease.

In none of these publications was the metabolism studied. Inasmuch as the metabolism of the monkey approaches somewhat closely that of man we decided to repeat these experiments.

Our first animal was used to make certain that we could reproduce the disease in our laboratory.

EXPERIMENT I.—A female *Macacus rhesus*, 6 pounds 5 ounces in weight, was placed on September 25, 1913, in an Abderhalden metabolism cage and kept in a bright, sunny, well-ventilated laboratory. The animal was in the best of health and spirits. It was placed on a general diet of bananas, peanuts and milk. The meals were given at regular intervals by the same laboratory attendant. On November 1, 1913, after five weeks had elapsed, in which to enable it to become accustomed to its surroundings and during which time it had maintained its weight (6 pounds 3 ounces), it was placed on a quantity of a dried milk preparation (The Merrell-Soule Skimmed Milk Powder, Syracuse, N. Y.), sufficient for its caloric needs. She lost progressively in weight until by February 12, 1914, she had lost 1 pound 7 ounces; on that date it was noted that she looked ill, had a poor appetite and was listless, sitting quietly in the corner of the cage; there was evident disability of the left arm and left leg, the former she nursed and the latter she dragged; there was distinct desquamation of the face and trunk, but there was no evident affection of the gums and no external hæmorrhages. In spite of the continuation of the dried milk food the monkey gradually regained weight and the other symptoms subsided.

She was therefore placed on condensed milk (The Ferndale Evaporated Milk) on April 17, 1914, at which time she weighed 5 pounds. On May 4, 1914, there appeared ecchymoses around the orbits and in the floor of the mouth, and swelling and blueness of the gums became evident. It was again noticed that she was constantly nursing her left arm and wrist and that she was more emaciated (4 pounds 10 ounces). There was some looseness of the bowels, but no melæna or hæmaturia. A skiagram on May 8 was negative. On June 8, 1914, one of the lower central incisor teeth fell out and the ecchymoses of the eyelids were more evident; slight conjunctival hæmorrhages too were seen; she then weighed 4 pounds 6 ounces. She became more and more inactive and could not be handled without evincing pain. On July 7, 1914, blood appeared in the stools. On July 9, 1914, she was chloroformed and skiagrams were taken which revealed the typical white line at the epiphyses of the wrist-joints with separation of the epiphyses at the lower end of both femora. Her weight was now 3 pounds 6 ounces or a loss of 46.6% of the body weight.

The autopsy by Dr. C. E. Royce* on July 9, 1914, revealed crepitation of the right wrist-joint. The lower left central incisor was missing and all the central and lateral incisor teeth were loose and readily extracted. The gums were bluish red but not appreciably swollen. The large intestine showed numerous areas of hæmorrhage and ulceration. The other abdominal and thoracic viscera were normal. The sternum and costo-chondral joints were normal. The epiphyseal regions at both wrists and elbow-joints showed marked softening and subperiosteal hæmorrhage, while several of the synovial cavities were filled with a bloody fluid. The lower extremities were less affected.

Microscopically.—The characteristic changes were found in the bones, namely, hæmorrhage into the marrow which frequently was of the "Gerüstmark" type, changes in the calcifying zone and an absence of cells in the intertrabecular spaces of the epiphyses which were often filled with red blood cells, and spindle cells. The sections from the viscera were normal with the exception of those from the large intestine, which showed amœbæ in the deeper portion of the mucosa and those from the liver and kidneys which presented a granular degeneration.

* We wish to express our thanks to Dr. C. E. Royce, pathologist to the University Hospital, for his interest and valuable assistance in the gross and microscopic study of our animals.

Anatomical Diagnosis.—Scurvy, with hæmorrhage and softening of the bones of the shoulder and pelvic girdle (except the clavicles) and extremities and the upper and lower alveolar processes; granular degeneration of the liver and kidneys; amœbic colitis.

Having successfully reproduced in every respect the classical picture of scurvy in its clinical and pathological aspects we next turned to the study of the metabolism. As there were no data in the literature on the mineral metabolism of the normal monkey Baumann and Oviatt studied this in our second animal and published their results in a separate paper.¹⁰ This second monkey was now submitted to the same conditions as the first and ran a similar course clinically and at autopsy showed the same changes.

EXPERIMENT II.—*Macacus rhesus* (male). This monkey was kept in the Abderhalden metabolism cage in the same laboratory from September 25, 1913, when it weighed 5 pounds 13½ ounces to January 21, 1915, when it weighed 6 pounds 3 ounces. It was then placed on a weighed diet of bananas and milk and the normal metabolism studied. On January 28, 1915, it was placed on a restricted condensed milk diet. It gradually developed loss of weight, loss of strength, bodily inactivity, alopecia, gingivitis, bloody diarrhœa and the other symptoms noted in the former experiment. On June 4, 1915, it was chloroformed, weighed and skiagraphed. The weight was now 4 pounds 8 ounces, a loss of 27.2% of the body weight. The skiagrams showed very definite white lines at the lower epiphyses of the tibiæ and radii, thinning of the bony tissue at the lower end of the humeri and femora with an increase in the density of the corticalis of all the long bones. (See Plates I and II.)

At the autopsy by Dr. C. E. Royce on June 4, 1915, there were noted alopecia over the thorax, swelling and hæmorrhages of the gums, and looseness of the incisor teeth. The lower ends of the radii and ulnæ were swollen and crepitated on pronation and supination. The thoracic and abdominal organs were negative except for an intussusception of the sigmoid and pallor and flabbiness of the heart muscle.

The fourth and fifth costo-chondral articulation on the right and the fifth and sixth on the left appeared redder than the others. The long bones of the four extremities showed even more marked changes than in the first experiment, brittleness being a marked feature, as well as separation of the epiphyses; subperiosteal and intra-articular hæmorrhages were frequent. The rami of the lower jaw showed marked subperiosteal hæmorrhages and fragility. The scapulæ and pelvic bones were also affected.

Microscopically.—The picture was similar to that in the former experiment, only that the lesions were more marked, particularly in the bone-marrow which was everywhere replaced by a homogeneous material.

Anatomical Diagnosis.—Scurvy with hæmorrhage and softening of the bones of the girdles (except the clavicles) and the four extremities, as well as the upper and lower alveolar processes; granular degeneration of the liver and kidneys; intussusception of the sigmoid with suppuration and necrosis.

The methods of feeding and of collection of the urine and fæces have already been described.¹⁰ We waited until the disease-picture was characteristic for scurvy before investigating the nitrogen and mineral metabolism. Three periods were studied, each period consisting of two consecutive days, except the third, when owing to the occurrence of diarrhœa or melæna two consecutive days feces could not be obtained. The third period therefore represents the urine and feces of two days nine days apart.

The methods of analysis were the same as those described before¹⁰ except that the total sulphur and sulphur partition were estimated according to Drummond's¹¹ modification of the benzidine precipitation method of Raschig.

The *nitrogen* loss that occurred coincides with our findings in the guinea-pig. This and the high urea content of the blood found by Lewis and Karr¹² in scorbutic guinea-pigs

Chlorine.—There is a tendency to chlorine retention, especially in the last period, when more than half of the ingested chlorine was retained.

The *phosphorus* metabolism was unusual throughout. The marked retention during the first two periods, followed by the relative high excretion in the urine during the third period, is difficult to explain.

TABLE I.

May, 1915.	Volume of urine in c. c.	Weight of dry feces in gm.	Total nitrogen.				Ammonia nitrogen of the urine.	Sulphur.					
			Intake.	Output.		Balance.		Intake.	Output.				Balance.
				Urine.	Feces.				Inorganic.	Etherial.	Neutral.	Feces.	
5 and 6...	361	4.29	3.2060	3.0671	0.2566	0.1177—	0.0809	0.1695	0.0858	0.0340	0.0251	0.0189	0.0057+
10 and 11...	385	8.74	3.2060	3.4500	0.5227	0.7667—	0.1721	0.1695	0.0868	0.0346	0.0305	0.0383	0.0207—
15 and 24...	242	9.36	3.2060	3.2586	0.5598	0.6124—	0.1606	0.1695	0.0909	0.0285	0.0325	0.0410	0.0234—
Daily av'ge.	164.3	3.73	1.6030	1.6293	0.2232	0.3495—	0.0689	0.0848	0.0439	0.0162	0.0147	0.0163	0.0064—
								Abnormal	58.6%	21.6%	19.6%	of T. S.	
								Normal..	60.9%	16.9%	22.2%	of T. S.	

May, 1915.	Chlorine.				Phosphorous.				Sodium.			
	Intake.	Output.		Balance.	Intake.	Output.		Balance.	Intake.	Output.		Balance.
		Urine.	Feces.			Urine.	Feces.			Urine.	Feces.	
5 and 6.....	0.6894	0.5146	0.0005	0.1743+	0.5686	0.0187	0.2188	0.3311+	0.2704	0.1855	0.0126	0.0723+
10 and 11.....	0.6894	0.5929	0.0011	0.0954+	0.5686	0.0229	0.4458	0.0999+	0.2704	0.2227	0.0258	0.0219+
15 and 24.....	0.6894	0.3089	0.0011	0.3794+	0.5686	0.1147	0.4774	0.0235—	0.2704	0.0872	0.0276	0.1556+
Daily average....	0.3447	0.2361	0.0004	0.1082+	0.2843	0.0260	0.1903	0.0680+	0.1352	0.0825	0.0110	0.0417+

May, 1915.	Potassium.				Calcium.				Magnesium.			
	Intake.	Output.		Balance.	Intake.	Output.		Balance.	Intake.	Output.		Balance.
		Urine.	Feces.			Urine.	Feces.			Urine.	Feces.	
5 and 6.....	0.8981	0.7279	0.0528	0.1174+	0.7318	0.1307	0.2475	0.3536+	0.0699	0.0196	0.0247	0.0256+
10 and 11.....	0.8981	0.7933	0.1080	0.0032—	0.7318	0.1250	0.5041	0.1027+	0.0699	0.0178	0.0503	0.0018+
15 and 24.....	0.8981	0.4576	0.1155	0.3250+	0.7318	0.1590	0.5399	0.0329+	0.0699	0.0199	0.0539	0.0039—
Daily average....	0.4490	0.3298	0.0490	0.0702+	0.3659	0.0691	0.2152	0.0815+	0.0349	0.0095	0.0215	0.0039+

possibly indicate an increased nitrogenous catabolism in experimental scurvy.

The *ammonia-coefficient* (4.2%) shows a slight increase above the normal figure (1.4%), but this is not to be considered indicative of an acidosis, especially when one bears in mind that the analyses were made several weeks after the collection of the urine.

The *sulphur* partition and balance are normal. It is of interest to note that the inorganic, ethereal and neutral sulphur formed 58.6%, 21.6% and 19.6%, respectively, in the scurvy period as compared with 60.9%, 16.9% and 22.2% of the normal period. These figures, then, are further confirmation of the difference in the sulphur partition of the monkey and that of man. It would be of interest to determine the sulphur partition of the urine of the higher apes.

Sodium and Potassium.—The retention of these elements during the third period parallels that of chlorine for this period.

Calcium and Magnesium.—Considerable quantities of calcium were ingested during the scurvy period and there was pronounced retention. During the previously reported normal period there was almost calcium equilibrium. The magnesium requires no comment.

CONCLUSIONS.

The changes in the mineral excretion of the monkey during the scorbutic period are not sufficiently significant to admit of easy interpretation.

The marked loss of the various mineral substances encountered in previous experiments with man and guinea-pigs was not observed in the present series.



FIG. 1.



FIG. 2.

We conclude that a study of the intake and output of the inorganic elements in human adult scurvy and the experimental scurvy of the guinea-pig and the monkey does not yield sufficiently decisive information to warrant an explanation of the pathogenesis of scurvy.*

* We wish to acknowledge our indebtedness to Dr. L. Baumann, director of the Medical Research Laboratory, for many valuable suggestions.

LITERATURE.

1. Baumann, L., and Howard, C. P.: Arch. of Int. Med., 1912, IX, 665.
2. Baumann, L., and Howard, C. P.: Am. Jr. Med. Sci., 1917, CLIII, 650.

3. Jackson, F. G., and Harley, V.: Lancet, 1900, I, 1184.
4. Hart, K.: Virchows Arch., 1912, CCVIII, 367.
5. Hart, C.: Jahrb. f. Kinderheilk., 1912, LXXVI, 507.
6. Hart, C.: Mediz. Klinik, 1913, IX, 221.
7. Hart, C.: Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1913, XVII, 24.
8. "Der Skorbutt der kleinen Kinder." Hart und Lessing, Stuttgart, F. Enke, 1913.
9. Talbot, F. R., Dodd, W. J., and Peterson, H. O.: Bost. M. and S. Jr., 1913, CLXIX, 232.
10. Baumann, L., and Oviatt, E.: Jr. Biol. Chem., 1915, XXII, 43.
11. Drummond, J. C.: Biochem. Jour., 1915, IX, 492.
12. Lewis, H. B., and Karr, W. G.: Jr. Biol. Chem., 1916, XXVIII, 17.

JOHNS HOPKINS AND SOME OF HIS CONTEMPORARIES.¹

By HENRY M. HURD, M. D.,

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The primary object of our Historical Club, when it was founded, was the study of medical history. To-night I have thought it wise to speak of the life of one who was not directly connected with the history of medicine, but who, because of the influence which the university and hospital he established have had upon medical education in this country, seems closely allied to medicine. I have also an additional reason for speaking briefly of his personal history before this club, because as the years pass I find that the career of Johns Hopkins becomes less familiar to the present generation, and there is danger that he may become a mythical personality. This is my reason for speaking of his origin and personal characteristics and giving some account of his career in Baltimore. I also wish to speak of his personal interest in the hospital and of the men he selected to carry out the enterprise.

According to an interesting research made some years ago by Miles White, Jr., a grandnephew of Johns Hopkins and at present one of the trustees of The Johns Hopkins University, the family of Johns Hopkins was of English descent, and came from England to Virginia about the middle of the 17th century. They were originally Puritans, driven from England by the persecutions to which they had been subjected prior to the accession of Charles II, and who had emigrated in company with many others of the same belief. They seem to have prospered for a time in Virginia, but were eventually compelled to remove to Maryland because of the restrictions placed upon them by the established church in Virginia, and also because there was great religious freedom in Maryland at that time.

The immediate ancestors of Johns Hopkins came to Maryland and settled in Anne Arundel County. Upon the Restoration in England, however, difficulties again arose, and again the Puritans were persecuted. Whether this had anything to do

with their adoption of Quakerism I am unable to say. It is a fact, however, that Lord Baltimore, when his estates were restored to him after the Restoration by Charles II, showed great tolerance toward the Quakers; and it is to be remembered that in England the Quakers and Catholics seem to have been persecuted alike, which may have been one reason why Lord Baltimore showed the Quakers special consideration. At any rate, from the year 1700 on the Hopkins family were all Quakers. In Maryland two yearly meetings were established, one at West River, in the vicinity of Annapolis for the Western Shore, and the other at Third Haven, or Tread Avon, on the Tread Avon River near Easton, for the Eastern Shore. About 1671 Maryland was visited by George Fox, the founder of Quakerism, who is known to have attended the yearly meetings on both the Western and Eastern Shores. A few years afterwards William Penn also visited both meetings. The statement is made, as tending to show the good feeling between Lord Baltimore and the Friends, that on one occasion, accompanied by members of his family, he visited a yearly meeting in order to witness the manner in which services were conducted. It should be remembered that the Friends had a very remarkable influence in the development of the states of Pennsylvania, Maryland and Virginia, and in Maryland at once became a growing and influential body.

Johns Hopkins was born May 19, 1795, at White Hall, his father's estate near West River in Anne Arundel County. He was a son of Samuel Hopkins, who was a grandson of the first Johns Hopkins, whose mother was Margaret Johns and whose father was Gerard Hopkins, born in 1700, who was probably a son of an earlier Gerard Hopkins who came from Virginia. Samuel Hopkins was born in 1759 and died in 1814. He was a Quaker and a member of the meeting which met at West River. He was married, however, at Fairfax meeting in Loudon County, Virginia, to Hannah Janney in 1792. Hannah Janney was born May 19, 1774, and was the daughter of Joseph and Hannah Janney. Samuel Hopkins

¹ Read before The Johns Hopkins Hospital Historical Club, Monday, March 12, 1917.

seems to have been considerably older than his wife, who was married at the age of 18. To Samuel and Hannah Hopkins were born 11 children, 6 sons and 5 daughters, all of whom grew up. Johns Hopkins was the second son. Of Samuel Hopkins it is said that he was "an upright, noble-minded man, polite, agreeable and entertaining in conversation, much beloved by his friends and acquaintances, useful in society, his neighborhood and family." Of Hannah Janney Hopkins it is recorded that "she was a woman of superior intellect and will and one of the guiding spirits of the Baltimore yearly meeting." Later in life, after she came to Baltimore to live, she became a preacher in the Society of Friends.

Many interesting details are given concerning Johns Hopkins as a boy. The family lived liberally upon a large farm and seem to have prospered. At one time the possession of slaves had enabled them to cultivate the farm with ease and to engage especially in the cultivation of tobacco, which required much care and heavy work. For many years, however, the Religious Society of Friends had become very much interested in freeing the slaves and had borne constant testimony against the holding of men in bondage as entirely inconsistent with their ideas of right. In 1812 the yearly meeting adopted a minute that no persons could remain connected with the meeting who held slaves. It is said that Samuel Hopkins was much troubled by this action, in view of his large family and the difficulty of managing his estate without the aid of slaves. He walked the floor at night in his perplexity, and finally came to the decision that he ought to emancipate his slaves, which he did in 1812. Such action on his part he knew would give rise to much criticism from his neighbors who still held slaves and to a loss of prestige and influence in the community. It was also practically impossible to secure any labor other than slave labor, and the step necessitated great changes in the duties and responsibilities placed upon himself and his sons by compelling them to do the work of the plantation.

Tradition states that Johns Hopkins was in the habit of walking to school, in company with his younger brothers and sisters, a distance of two miles, and that he exercised a supervision over the other children and was in many ways regarded as a leader among them.

In 1812 he obtained a position in the store of his uncle, Gerard T. Hopkins, in Baltimore, where he was employed for several years. Gerard Hopkins was also a Friend and a preacher.

Baltimore, at that time a new city in Maryland, was a comparatively insignificant town. It was not incorporated as a city until 1796, when large additions were made to its limits, as is shown by the fact that in 1790 it contained 13,503 inhabitants, whereas by 1800 the number had increased to 31,514; by 1810 it had increased to 46,555, and by 1820 to 62,738. This indicates that Baltimore had a comparatively slow growth—about fifteen or sixteen thousand inhabitants in each decade. It was, however, a city of considerable commercial importance. Tobacco was extensively grown in Maryland, and Baltimore was the great shipping port for this

product. It was also a shipping port for grain and flour to the West Indies and South America. Many of the streams, like the Patapsco, Jones's Falls and Gwynn's Falls, had large flour mills upon their banks run by water power, where wheat, then extensively grown in the region, was converted into flour. In many instances in order that the flour might be transported to South America in comparatively slow sailing vessels without danger of spoiling, bakeries were established in connection with flouring mills and a large proportion of the flour was baked into ship biscuit to supply these hot countries. There was also an extensive trade with the West Indies in sugar and with South America in coffee. During the Napoleonic wars there was also an extensive trade in neutral products with the European countries and particularly with the armies in Spain. The commercial activity of Baltimore, therefore, was very extensive. During the War of 1812 many of the sailing vessels, which operated between Baltimore and the Southern ports, were converted into privateers. In scanning the list it is apparent that more privateers sailed from Baltimore than from either New York, Philadelphia or Boston. The manner of life of the city itself was not unlike that of ordinary seaport towns. Very little was done in an educational way except by private initiative, and the same is true of philanthropic and charitable work. It was essentially a commercial city and its intellectual activity was largely in the line of business. It was a thriving, bustling seaport town, with many characteristics which had been derived from early settlers, who were largely from Scotland or the north of Ireland and engaged in commercial or shipping pursuits.

After five years of apprenticeship in his uncle's store Johns Hopkins established a grocery business for himself. His father died in 1814, and tradition states that at the time of his death several crops of tobacco had accumulated on the plantation near West River on account of the embargo of 1807, and these his mother, who managed the farm, sold at a good price at the close of the war and placed the money in his hands, for which he paid her interest, and which enabled him to begin business on his own account. We know little about his business habits, but it is evident that from the beginning he was an active, efficient and prosperous man. At first the firm was Hopkins and Moore. Subsequently two of his brothers and a cousin were associated with him. He does not seem to have had any domestic life until after 1832, when in consequence of an attack of cholera which nearly cost him his life he gave up living in a hotel on Baltimore Street and purchased a house on Franklin Street, which he occupied with his two brothers, one of whom was fatally injured in riots which disgraced Baltimore about 1835 by reason of the dissatisfaction of the populace with the failure of several important banks. The house on Franklin Street was occupied by Johns Hopkins until 1843, when his mother, failing in health, came with two of his sisters to reside with him, and a larger house was purchased on Lombard Street, where all lived until his mother's death in 1849. Mr. Hopkins then purchased the house immediately opposite the Hotel Rennert, which with his two sisters he occupied for the remainder of his life. About 1844

he purchased an estate known as Clifton. He rebuilt the house and made great improvements on the property, establishing greenhouses, planting trees and in many ways making it an ornamental park. For many years, in fact, it was the most conspicuous park in Baltimore and was regarded as a show place.

Johns Hopkins had only the education which was available at the country school in Anne Arundel County, but it must be borne in mind that the country schools in many parts of Maryland were superior to the schools which existed elsewhere. The prosperity of the colony, largely due to the sale of tobacco, early brought many Englishmen of excellent education to Maryland in search of fortune. Many of them had met the usual fate of such adventurers and were compelled to engage in teaching. There is a tradition that the school which Mr. Hopkins attended during his boyhood was taught by a scholarly man who had been a student at Oxford and was far beyond the ordinary average of teachers in country schools. The statement is also made that his father, Samuel Hopkins, was a man of much reading, who regularly supervised the education of his son, especially in the study of history, reviewing with him the work of the school at the close of every week in the presence of the family. It was the custom of Friends then and for many years afterwards to read the best books and to spend quiet evenings at home in reading and study. The library which Johns Hopkins bequeathed to The Johns Hopkins Hospital was an unusually large and well-selected one, particularly rich in historical and economic works. Johns Hopkins seems to have been all his life a diligent reader and to have profited by the knowledge which he obtained in this way.

His business training was acquired precisely as such training came to many other young men of the time. In the store of his uncle he performed the usual work, such as sweeping, unpacking goods and such general utility work as was then expected of all employees. It is evident from the accounts which are given that as long as he remained in business he was diligent as to hours and careful as to the extent of the responsibilities which he assumed. When he retired from business in 1847 he became connected with various large enterprises, such as banks, coal-mining companies and transportation companies, and was able by reason of his business experience, sagacity and intuitive perception of the character and possibilities of young men to give them timely pecuniary assistance. The statement has been made again and again by men who secured credit through his assistance, that they owed their ultimate business success to the help which he gave them. There are traditions that upon discount day at the different banks with which he was connected as director he often established the credit of comparatively unknown persons by affixing his personal signature to the paper of young men whose prospects of success were not apparent to his fellow directors, and that generally the men thus assisted became successful and prosperous business men, largely through the credit thus extended.

In the matter of personal character it is evident from the information which can be obtained that Mr. Hopkins was a man of large views and broad vision. He foresaw the importance to the city of Baltimore of the Baltimore and Ohio Railroad, and on two occasions advanced large sums of money, one to extend the railroad at an early date and the other to maintain its credit during the panic of 1873, when it was largely through his influence that Baltimore's credit was sustained and the city did not suspend payment of debts, as did many other cities. He arrived at his conclusions rapidly and intuitively, but his judgment was extremely sound. His physical health is said to have been not of the best, and following the attack of cholera in 1832 he suffered during the remainder of his life from insomnia and various digestive difficulties. The statement is made that the companionship of his favorite sister, who kept his house and looked after his diet and who always remained up at night until he returned home, to welcome him and talk over the affairs of the day, was of great service to him. He was fond of children, fond of his nieces and nephews, and given to hospitality. Religiously he was brought up in the Religious Society of Friends, but was not a member of the Society. He remained, however, essentially a religious man, and gave liberally to the support of the meeting, which he at times attended. His charities also were numerous, and at his death many old friends and business acquaintances were found by his executors to have been in receipt of regular allowances from him, of which the recipients alone knew the source. He was also generous to his relatives and friends.

He was unusually fond of country life, and at Clifton was able to gratify his taste by the improvement of his estate there. He planted the grounds with exotic trees of many rare varieties, had large and beautiful greenhouses, and indulged in the tastes which are available only to those who possess abundant means.

He was connected with many charitable and financial boards and assumed his share of the duties and responsibilities which attach to such work.

It is interesting to note that many persons have honestly thought they were influential in inducing Mr. Hopkins to devote so large a portion of his fortune to the establishment of the Hospital and University. It is evident that he had the matter much at heart, and was in the habit of talking with persons whose judgment he valued as to the disposition of his property. Francis T. King once said in a public address that Johns Hopkins had a strong conviction that his large fortune was given to him not for his own pleasure, but to accomplish some great work, and that it was his duty to make such use of his stewardship, as Mr. King expressed it, that it might continue to do good after his death. It is probable, therefore, that he conversed with many and received much advice. I have always believed that the example of George Peabody, of London, a former resident of Baltimore, who established the Peabody Institute and who devoted a large sum of money to education in the South, had great influence in leading Johns Hopkins' thoughts toward the establishment of an educa-

tional institution. The late President Gilman believed that several conversations held by Mr. Hopkins with Dr. Joseph Parrish, of Philadelphia, a member of the Society of Friends, had much to do with his ultimate design to establish a hospital and university. Dr. Parrish is reported to have said that as long as the world existed there would be sick people to care for and ignorant people to educate and that for this reason Mr. Hopkins would do well to establish a hospital and a university.

Johns Hopkins had perfected his plans a number of years before his death. Thus, he incorporated both the university and hospital in the year 1867, but neither institution had a full organization of its board until some years later. The original incorporators of the hospital were the following 12 named men, several of whom died before the formal organization of the board. These men were mostly business associates and personal friends of Mr. Hopkins or members of the Religious Society of Friends.

Francis T. King was designated by Johns Hopkins to be president of the board of trustees. Mr. King was a native of Baltimore, whose father came from England. He was educated at St. Mary's Seminary and had been engaged in various business enterprises. He was prominently connected with the Religious Society of Friends and for more than 20 years was clerk of the meeting. He was also interested in philanthropic enterprises, especially those in his own denomination. Later in life he occupied prominent positions in connection with two savings banks. He possessed energy, enthusiasm and great faith in the future of Baltimore. He had large plans, and with firmness of purpose and great patience was able to see most of them realized.

John W. Garrett, former president of the Baltimore and Ohio Railroad and a personal friend of Mr. Hopkins, was a man of great executive capacity and business ability. He was associated with Mr. Hopkins in many enterprises, and unquestionably had great influence with him. It is said he induced him to give a large sum of money to the Young Men's Christian Association to enable it to clear off the debt upon its building, at a time when Mr. Hopkins had lost several hundred thousand dollars in a mining enterprise.

Judge George W. Dobbin, who had been a judge of the superior court for a number of years, was an efficient member of the board. He was well known and respected for his probity, elevation of character and devotion to the public service. He served the university and hospital for many years and died at an advanced age, after the opening of both.

Galloway Cheston was a manufacturer, a member of the Society of Friends and prominent in financial circles in the city. He was a director of the Baltimore and Ohio Railroad, and a trusted associate of Mr. Garrett. His large fortune was acquired by the possession of flour mills, several of which were situated in the vicinity of Baltimore on Gwynn's Falls. He had excellent ideas as to organization and building and was personally interested in the plans of the hospital.

Thomas M. Smith was a merchant and a personal friend of Mr. Hopkins. His appointment seems to have been made

because of his pleasing personality. I cannot find that he contributed in any great degree to the plans of the hospital.

William Hopkins was a cousin of Johns Hopkins and a merchant much respected.

Francis White had married a niece of Mr. Hopkins, and was one of the executors of his estate. He was also a trustee of the University. His services to the Hospital and the University were of great value and continued for many years. He had an attractive personality and made many friends. He lived to an advanced age and served both foundations faithfully and wisely.

Lewis N. Hopkins was a nephew of Johns Hopkins and had always been a great favorite with his uncle. He was a commission merchant, but during the last few years of his life was city collector. He had an intimate knowledge of his uncle's plans and was a trustee of both the Hospital and University.

Dr. Alan P. Smith was a grandson of Nathan Smith, who was a well-known physician in New England and whose life was spent in promoting medical education there. Nathan Smith was connected with four different medical schools, three of which he founded and in all of which he did very valuable work. His son, Nathan R. Smith, came to Baltimore, and was the leading surgeon in this city. Alan P. Smith, a son of the latter, was a surgeon of ability. He was the family physician of Johns Hopkins.

Dr. John Fonerden was the resident physician at the Maryland Hospital for the Insane, which stood on the site now occupied by The Johns Hopkins Hospital. Johns Hopkins was one of the board of visitors of this institution, and probably the association of the two in connection with the Maryland Hospital suggested his appointment as a trustee. He died prior to the organization of the board.

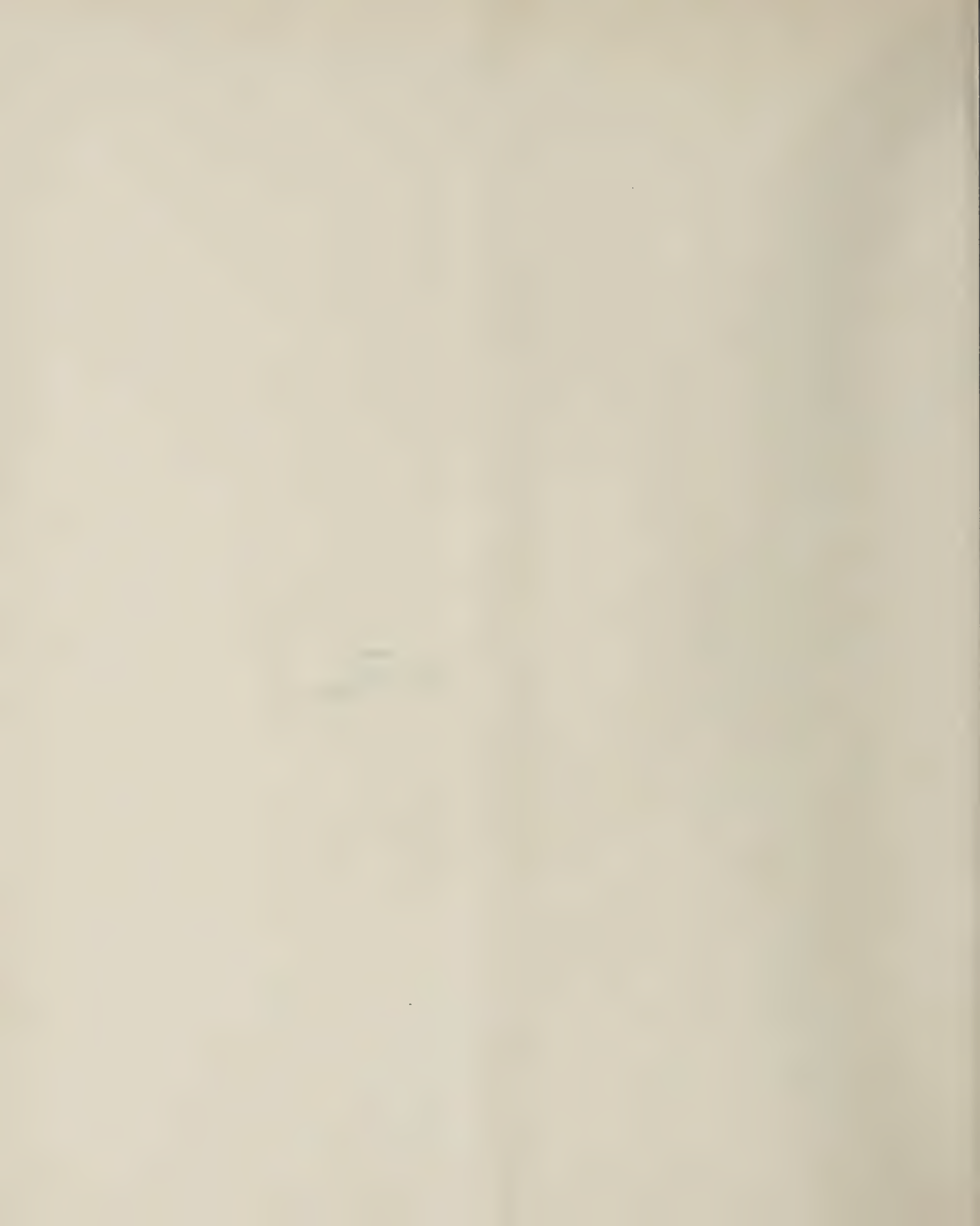
Charles J. M. Gwynn was a distinguished lawyer of Baltimore. He was counsel for almost all the large corporations of the city during some portion of his life. He was also the legal adviser of Mr. Hopkins, drew his will, and prepared the acts of incorporation of the Hospital and University. He served upon both boards faithfully for many years and both institutions owe much to his legal ability.

Richard M. Janney had married a sister of Johns Hopkins. He was at first a merchant and manufacturer, but during the last years of his life was occupied wholly in philanthropic work. He was much interested in the welfare of negroes who had been emancipated by their masters and who needed aid and education. He also took an active part in the establishment of schools for colored people at the close of the war and after their general emancipation. He was interested in the work of the Freedmen's Bureau in the South, and also was instrumental in establishing the Prisoners' Aid Society and a children's aid society, which afterwards became the Henry Watson Children's Aid Society. He, too, died before the Hospital board was organized. Mrs. Francis White was a daughter of Mr. Janney.

It is evident that these men were close acquaintances of Mr. Hopkins and familiar with his views and wishes as to the organization of the hospital. There is reason to think, from



John Hopkins



a careful reading of the letter prepared by him for the instruction of his trustees, that he had more definite views as to the organization of the Hospital than of the University. I have heard it said that the University trustees, in the organization of that institution, were often at a loss to know whether

they were fully carrying out the will of the founder. In the organization of the Hospital there was, however, no reason for such apprehension. The clear-cut, enlightened and advanced views of Mr. Hopkins have served as a guide and have contributed materially to its advancement and prosperity.

PRESENTATION OF THE MEDALLION PORTRAIT OF DR. RUPERT NORTON.¹

DR. HURD: Our first duty to-night is to pay a tribute to a friend who we all loved and honored, and whose replica, which we shall see for the first time to-night, will always bring up many pleasant memories, and of course many sad ones. I think we can all rejoice that the affection of a devoted wife, together with the suggestions and recollections of relatives and friends and, above all, the expression of the artistic feeling of Mr. Victor Brenner, have reproduced our dear friend who has gone.

DR. W. S. THAYER: 'Twas an interesting group of men—the little family that constituted the House Staff of The Johns Hopkins Hospital during the years which passed before the foundation of the Medical School and before the days when we began to call on our own graduates to fill the internships.

They were gathered from many schools—Lafleur and Hewetson and Barker and Cullen and Fitcher and McCrae from Canada; Robb and Scott and Toulmin and Ghiskey and Farr and Bloodgood and Russell and Clark and Ramsay and Oppenheimer and Edwards from the University of Pennsylvania; Brockway and Parker and Lazear from New York; Nuttall and Blumer from California; Flexner from Louisville; Young and Huger and Block and Hoke from the University of Virginia; Councilman and Abbott and Clark and Reese and Baltzell and Simon and Hoch and Smith and Van Ness and Atkinson and Stokes and Walker from the University of Maryland; Phippin and Norton and Cushing from Harvard; Whitman from Paris; Broedel and Werckmeister from Germany—to mention only a part.

Few of us remain to-day to walk the familiar corridors, to keep alive the fading traditions and to welcome the old companions as they return from time to time from all parts of the world to edify us with their wisdom and, alas, to surprise us by their maturity. But there are some who come back to us often, who never change, whose eyes are as clear, whose step is as light, whose voices are as fresh as they were 25 years and more ago. Brockway and Scott and Reese and Hewetson and Livingood and Edwards and Oppenheimer and Ramsay and Lazear and Whitman—they can never grow old.

There is another, peculiarly dear to those of us who remain because we have of him a double memory—a memory of his youth in which he first left us, and of his prime in which we possessed him again.

Rupert Norton came to us in 1893 as a member of the Medical Staff, and remained with us for over two years. His

work as a house officer was systematic, painstaking and thorough. As one reads to-day the records written in his neat and careful hand, the evidence of the character of his work is clear. Then came the years of his Washington practice, interrupted by the Spanish war, when he volunteered immediately as an acting assistant surgeon. At the end of the war came a period of years during which he was Medical Director of the New York Life Insurance Company in Paris, and then, in 1906, he came back to us again as Acting and Assistant Superintendent. From that time to the day of his death he devoted all his energies to the interests of the Hospital.

Among the past members of the staff few have been dearer to their associates. Norton was not one of those who made friends at first glance. He was so modest, so retiring, so diffident that some who met him casually mistook his shyness for coldness. No one who met him for the first time could have fancied the depth of his feeling, the vigor of his enthusiasm, the inflexibility of his determination, the inherent courage of the man. But wherever Norton was closely thrown with anyone he left a friend, and usually a devoted friend. The warmth of friendship that he inspired was but a reflection of his own loyalty. He was one on whom his friends could depend wholly; and while with regard to himself misunderstanding or false report stirred him little, yet nothing was so sure to excite in him an immediate and almost fiery resentment as a misrepresentation or a slighting statement about a friend.

He recognized unfailingly and appreciated deeply real merit in whatever garb it was clothed, and he was remarkably tolerant of the failings and weaknesses of others. But he had little patience with snobbishness or pretence and he was quick to detect and resent insincerity or indirectness.

I have sometimes regretted that one possessed of such admirable qualities of the heart—qualities which so endeared him to his friends—should not have given more of his life to a practice in which this human influence might have made itself more widely felt. To those who knew him well the memory of these qualities is a very dear possession. Of his generosity I have spoken elsewhere. Not many, even among his closest acquaintances, realized the extent of his kindly charity.

During his later years in the Hospital his wise advice and counsel were much valued by all who surrounded him.

Few men are quite certain of themselves. However steadfast one may be in his highest aspirations, however deep one's devotion to principle, who, at the bottom of his heart, has not known a lurking anxiety lest, in the great emergency, his action might fall somewhat short of his ideal? He who has

¹ Johns Hopkins Hospital Historical Club, March 12, 1916.

witnessed the too common frailty of his fellows, how has he not meditated on what his impulse might be in the moment of supreme temptation or danger?

But there are some men who inspire their friends with a peculiar sense of stability and solidity; some in whom we cannot imagine a weak or a mean or a cowardly impulse; some men of whom we feel absolutely sure. Such a man was Norton, and of his life we may say in the words of the wise old philosopher: "*. . . meliorem illi vitam reddidit quam accepit: exemplar boni viri posuit; qualis quantusque esset ostendit: si quid adjecisset, fuisset simile praeterito.*" (Seneca, Epistola 93.) "*. . . for he hath returned a better life than he received. He hath set downe the patterne of a good man: he hath shewed what an one and how great he was: if he had added anything, it had beene like unto that which was past.*" (Lodge's translation, London, 1614.)

It is well that we should seek to perpetuate the memory of such men—that we should endeavor in bronze, in marble or in color to fix the impalpable and elusive inspiration that emanates from their presence. For the face of a good man is a benediction. And Norton's presence is with us now. One who knew him and loved him well, Victor Brenner, the distinguished sculptor, has brought back his calm and dignified and thoughtful features. And Mrs. Norton, who has herself a double claim to our affection as a graduate of our own training school for nurses and as his wife, has asked me to present this medallion to the institution to which he gave the best years of his life.

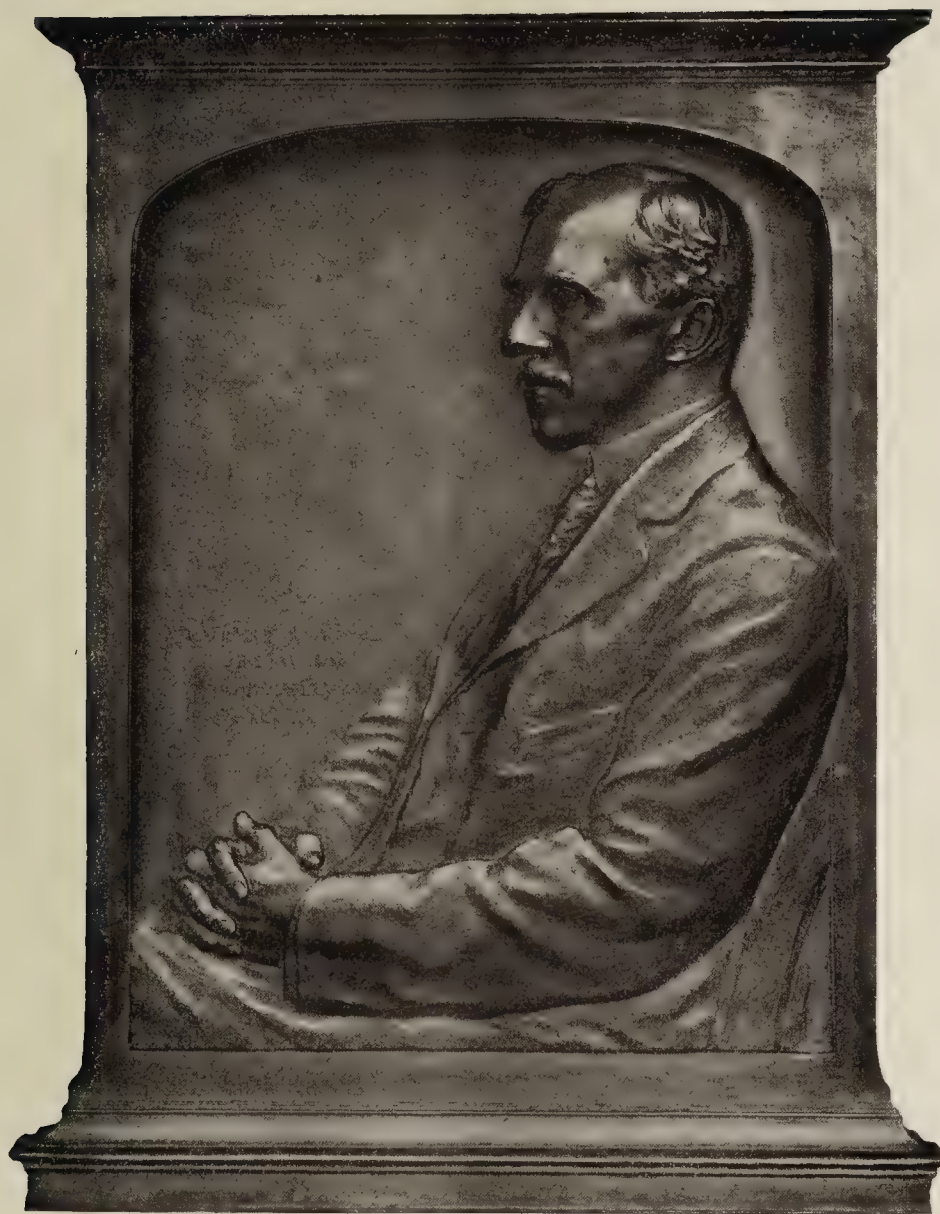
So may his face and figure continue to look out upon those who follow us—the face and figure of one whom we who knew him, love to recall—as has been set forth upon this plate—as physician, counsellor and friend.

JUDGE HARLAN: Serious purpose, fidelity to duty and loyalty in service are splendid qualities, and it was these qualities that the trustees of The Johns Hopkins Hospital recognized as dominating the life of Rupert Norton while he was connected with this institution—a connection which was all too short, owing to his untimely and pathetic death. What has been so well said by Dr. Thayer in appreciation of the life, of the services and of the character of Dr. Norton has found, I am sure, a response in the hearts of all of us, certainly in the hearts of the trustees. It is my great privilege, Mrs. Norton, on behalf of the Board of Trustees to accept this beautiful medallion portrait of our friend and to say that it will be placed among our most prized possessions, in order that it may be, not only for us but for those who come after us, a perpetual memory of one who lived a life of usefulness to this institution, of loyal, devoted and helpful service. He won the regard of all; he won the esteem of many; he won the love of those who knew him best.

DR. WELCH: There seems little to add to the beautiful tributes that have already been paid to the memory of our dear friend Rupert Norton. Each one who has spoken had used one word, which I think expresses the characteristic that comes first to mind when we think of Rupert Norton. Anyone

who is familiar with Josiah Royce's book on loyalty knows all that that characteristic signifies when it is applied properly to a human being. Rupert Norton was loyal to his family, to his friends and to his duty. He was loyal to the right as he saw it—and he saw it very clearly. Dr. Thayer called to mind the early group of enthusiastic young workers who came here at the opening of the Hospital and before the Medical School was opened, and Rupert Norton belongs in that most interesting and really remarkable group. They are all devoted to his memory, and among them I think he made some of the closest friends of his life. Almost the last words from him that appear in print—and it is something of a coincidence, I think, that they appear in the number of our BULLETIN which contains Dr. Thayer's "In Memoriam" to Rupert Norton—were spoken at a memorial meeting in honor of Dr. Billings, who was a close friend of Dr. Norton and who also belonged in that early group. In his tribute to Dr. Billings he has chosen to emphasize just those qualities which applied most surely to himself—he emphasized the real solidity and straightness of the man, the hatred of all shams, the really getting to the heart of things. Dr. Norton, I think, exemplifies also a characterization of the educated man that was made by a colleague—William James, a great philosopher—who speaks of the value of higher education to lead men to know what is good in life, what is good in persons, what is good in art and in literature.

Rupert Norton came from a family and an atmosphere which really constitute memories cherished by all of us in America, and which must have had a great influence upon him. He had an unostentatious exterior, a reserve that may at times have seemed brusqueness, but there was behind it, as there is often behind the outward demeanor of a reserved man, a heart all kindness and generosity and a certain genius for friends and friendship, and he linked close to him the few who penetrated the outer shell and got to the heart of the man. He began his professional life on the resident staff of Dr. Osler's service, and later spent three years in professional life in Washington, during which period he contributed over half a dozen papers to different medical publications. He enlisted at the outbreak of the Spanish-American War, and served throughout in one of the southern camps. After the war he went to Paris, where he held a position as medical director of an insurance company. He returned to Baltimore in 1906, at the time when Dr. Hurd took his long and well-deserved vacation. It was then I came to know him best. I soon learned that here was a man faithful in the discharge of his duties, filling a difficult position and filling it well. I was impressed then with his courage, with his patience under difficulties and with his determination to do the best for the service of the Hospital and the patients. He remained with us until the time of his death, and I think we all came to hold him in the highest esteem, and those of us who knew him best continue to have a very deep affection for him. He wrote some valuable papers on hospital organization. In a word, I think we can say that he has made contributions to all the different aspects of his work, first as an interne, then as an expert in life insurance



MEDALLION PORTRAIT OF DR. RUPERT NORTON.
BY VICTOR D. BRENNER.

matters, and then as a trained superintendent of a hospital, contributions that were entirely creditable, and that he gave promise of additional contributions had his life been spared. Dr. Thayer has spoken for his friends; Judge Harlan has spoken for the trustees of the Hospital, and if I may be allowed I will speak for the older group concerned in the organization and planning of the Hospital. We too are proud of this younger group of men. We cherish the memory of men like Rupert Norton, and it is well that his memory should be cherished here where he spent the best part of his life. He would probably have been surprised to know that we would hold a memorial meeting for him here, but we love to hold it and we are very grateful indeed to you, Mrs. Norton, for giving us this great privilege.

DR. HURD: There is one aspect I think in which Dr. Norton was preëminent, and that is as a literary man. He had literary instincts, a literary facility, and he also had a remarkably quick judgment as to literary form and taste. I have always felt that eventually he might have filled a high place in medical journalism. Few are capable of doing medical journalism as it ought to be done. Within two or three weeks of his sad and untimely death I received word from two different quarters, from editors of journals, that they had been going to offer him an editorial position. One of them was the most important medical journal in the country. I am sure that had he lived he might have found a career in medical journalism which he would have enjoyed. His heart was in that sort of work and he did it exceptionally well.

NOTE ON BOOKS GIVEN TO THE JOHNS HOPKINS HOSPITAL BY DR. HUGH H. YOUNG.

By C. W. G. ROHRER, M. D.

The publications on genito-urinary surgery and allied topics, donated by Dr. Hugh H. Young, to the library of The Johns Hopkins Hospital, comprise a total of 567 bound volumes, 35 dissertations, 17 monographs and 494 reprints. For convenience of reference, these books and pamphlets may be subdivided into the following groups:

Bound volumes, including text-books, treatises, atlases, descriptive and illustrated catalogues, biographical sketches of eminent surgeons, etc., 567.

German dissertations, 35.

Monographs (mostly French), 17.

Reprints, 494.

The splendid array of text-books and treatises forms by far the largest and most important part of the collection. It is interesting to note that in this group are contained a number of books of real historical value. One of the first is "A Treatise of Venereal Diseases," a quarto volume by John Astruc (1684-1766), translated from the last Latin edition and published in London in 1754. Another is "A Treatise on Gonorrhoea Virulenta and Lues Venerea," by Benjamin Bell (1749-1806), a two-volume work published in Edinburgh in 1793. A third is the interesting collection of "Letters Concerning the Diseases of the Urethra," by Sir Charles Bell (1774-1842), published in 1810.

The works of Jean Civiale (1792-1867), the celebrated French surgeon, who applied the process of lithotripsy to the destruction of urinary calculi, also grace this collection. Here, too, are found the "Observations on the Structure and Diseases of the Testis," by Sir Astley Cooper (1768-1841), a folio volume published in 1830 and embellished by 24 plates; and "A Practical Treatise on the Diseases, Injuries and Malformations of the Urinary Bladder, the Prostate Gland and the Urethra," by Professor Samuel D. Gross (1805-1884).

This collection also contains a splendid copy of "Practical Observations on the Treatment of the Diseases of the Prostate

Gland," by Sir Everard Home (1756-1832), John Hunter's brother-in-law. Home's work consists of two octavo volumes illustrated by copper plates from drawings made by William Clift, Hunter's last apprentice.

A book by William Cockburn entitled "The Symptoms, Nature, Cause and Cure of a Gonorrhoea," is of especial interest. This book, published in London in 1719, is the first medical work in which a colored copper plate was used.

A reprint of two tracts by Jean Paul Marat (1744-1793), a French revolutionist, is an exceptionally rare production. The first is "An Essay on Gleet." These tracts were printed for private circulation only, the edition consisting of 84 copies. The complete works of Philip Ricord and of Sir Henry Thompson are also of unusual interest and value, both from a historical and a clinical standpoint. Ricord was the first to establish the duality of gonorrhoea and syphilis; Sir Henry Thompson was famous for his work on the prostate and on stone in the bladder.

Reference should be made to the several treatises on anatomy and surgery, especially those published early in the eighteenth century. For example, the collection contains a copy of William Cheselden's "Anatomy of the Human Body," to which is added "A Short Historical Account of Cutting for the Stone." Cheselden (1688-1752) was an eminent English surgeon and anatomist, whose dexterity in lithotomy excited the wonder of his contemporaries. He preferred the lateral operation, performing it in 54 seconds of time.

The different editions of the works of John Hunter (1728-1793), the founder of scientific surgery, are well represented. The works of Malgaigne and the more modern works of Guyon, both celebrated French surgeons, add much to its value. The works of American surgeons—Senn, Gross, Bumstead, Taylor and others—occupy conspicuous places in Dr. Young's collection.

The early volumes of several important journals have been added: *Annales des Maladies des Organes Génito-Urinaires*,

Vols. I-XXI, 1883-1903; Association Française d'Urologie, Vols. I-XI, 1896-1907; Internationales Centralblatt für die Physiologie und Pathologie der Harn- und Sexual-Organen, Vols. I-X, 1889-1899; Centralblatt für die Krankheiten der Harn- und Sexual-Organen, Vols. XI-XVI, 1900-1905; Monatsberichte für Urologie, Vols. VI-XI, 1901-1906.

Mémoires de l'Académie Royale de Chirurgie, Vols. II, III, VI-XV, 1771-1774, and A Descriptive and Illustrated Catalogue of the Calculi and Other Animal Concretions Contained in the Museum of the Royal College of Surgeons in London, 1842-1845, Supplement I, by Thomas Taylor, 1871, 3 vols., should be also mentioned.

Several important works on anatomy have been included. Among these is the American edition of John and Charles Bell's treatise entitled "The Anatomy of the Human Body," a famous English text-book originally published in four volumes.

Among works of a biographical nature, in Dr. Young's collection, we find a copy of "Sketches of the Character and Writings of Eminent Living Surgeons and Physicians of Paris." Translated from the French of J. L. H. Peisse by Elisha Bartlett, M. D., it was published in Boston in 1831. The book contains nine biographical articles, beginning with Dupuytren and ending with Civiale.

A similar but larger work, appearing 12 years later (1843) than Peisse's book, has also been added. It is Dr. F. Campbell Stewart's volume, entitled "The Hospitals and Surgeons of Paris. An Historical and Statistical Account of the Civil Hospitals of Paris; with Miscellaneous Information, and Biographical Notices of Some of the Most Eminent of the Living Parisian Surgeons."

BOOKS GIVEN TO THE JOHNS HOPKINS HOSPITAL LIBRARY BY DR. HUGH H. YOUNG.*

ACTON, W.

Prostitution considered in its moral, social and sanitary aspects, in London and other large cities and garrison towns. 2. ed. London, 1870. 8°. The functions and disorders of the reproductive organs. 6. ed. Phila., 1875. 8°.

AMBARD, L.

Physiologie, normale et pathologique des reins. Paris, 1914. 8°.

AMERICAN COLLEGE OF SURGEONS.

A list of fellows. Chicago, 1913. 8°.

AMERICAN JOURNAL OF UROLOGY.

Vols. 1-5, 1904-1909. New York. 5 vols. 8°.

AMERICAN MEDICAL ASSOCIATION, TRANSACTIONS.

Section on genito-urinary diseases. Chicago, 1914-1915. 2 vols. 8°. Section on surgery. Chicago, 1914. 8°. Section on surgery and anatomy. Chicago, 1903-1912. 10 vols. 8°.

ANNALES DES MALADIES DES ORGANES GÉNITO-URINAIRES.

Vols. 1-14, 16-21, 1883-1896, 1898-1903. Paris. 20 vols. 8°.

ANNALS OF SURGERY.

Vols. 31-43, 1900-1906. Phila. 13 vols. 8°.

ARCHIVES UROLOGIQUES DE LA CLINIQUE DE NECKER.

Vol. 1, 1914. Paris. 4°.

ASSOCIATION FRANÇAISE D'UROLOGIE.

Vols. 1-11, 1896-1907. Paris. 11 vols. 8°.

ASTRUC, J.

A treatise of venereal diseases. Transl. from the last Latin ed. printed at Paris. London, 1754. 4°.

BAILLIE, M.

A series of engravings, accompanied with explanations, which are intended to illustrate the morbid anatomy of some of the most important parts of the human body. 2. ed. London, 1812. Fol.

BALLENGER, E. G.

Genito-urinary diseases and syphilis. 2. ed. London, 1914. 8°.

BARTHOLOW, R.

Spermatorrhœa; its causes, symptoms, results and treatment. 4. ed. New York, 1879. 8°. A practical treatise on materia medica and therapeutics. 7. ed. New York, 1893. 8°.

BASTIANELLI, R.

Studio etiologico sulle infezioni delle vie urinarie. Roma, 1895. 8°.

BAZY, P.

Maladies des voies urinaires. Séméiologie. Paris [n. d.]. 16°.

BEALE, L. S.

Urinary and renal derangements and calculous disorders. Phila., 1885. 12°.

BELHOMME, L., and MARTIN, A.

Traité pratique et élémentaire de pathologie syphilitique et vénérienne. Paris, 1864. 16°.

BELL, B.

A treatise on gonorrhœa virulenta and lues venerea. 2 vols. Edinburgh, 1793. 8°.

BELL, C.

Letters concerning the diseases of the urethra. London, 1810. 8°. The same. Boston, 1811. 12°. A treatise on the diseases of the urethra, vesica urinaria, prostate, and rectum. London, 1820. 8°. Illustrations of the great operations of surgery, trepan, hernia, amputation, aneurism, and lithotomy. London, 1821. 4°.

BELL, J.

Engravings of the bones, muscles and joints. First Am. from the second London ed. Phila., 1815. 4°.

BELL, J. and C.

The anatomy of the human body. 4 vols. in 2. New York, 1809. 8°.

BELMAS, D.

Traité de la cystotomie sus-pubienne. Paris, 1827. 12°.

BICKHAM, W. S.

A text-book of operative surgery. Phila., 1903. 8°.

BIERKOWSKI, L. J.

Anatomisch-chirurgische Abbildungen nebst Darstellung und Beschreibung der chirurgischen Operationen nach den Methoden von v. Graefe, Kluge, und Rust. Berlin, 1827. Fol.

BIGELOW, H. J.

Litholapaxy; or, rapid lithotripsy with evacuation. Boston, 1878. 8°. I. The mechanism of dislocations and fractures of the hip. II. Litholapaxy; or, rapid lithotripsy with evacuation. Boston, 1900. 8°. Orthopedic surgery and other medical papers. Boston, 1900. 8°.

BIRNBAUM, R.

A clinical manual of the malformations and congenital diseases of the fetus. Transl. by G. Blacker. Phila., 1912. 8°.

BOECK, W.

Erfahrungen über Syphilis. Stuttgart, 1875. 8°.

BOECKEL, A.

Valeur de la néphrectomie dans la tuberculose rénale. Paris, 1912. 8°.

BONAMY, C., BROCA, P., and BEAU, E.

Atlas d'anatomie descriptive du corps humain. 2. partie. Cœur, artères, veines, vaisseaux lymphatiques et aponévroses. Paris [1844]. 4°.

BOURDILLAT, H.

Calculs de l'urèthre et des régions circonvoisines chez l'homme et chez la femme. Paris, 1869. 8°.

BOYER, A.

Traité des maladies chirurgicales et des opérations qui leur conviennent. 4. éd. Paris, 1831. Vols. 8, 9, 10. 8°.

BREWER, G. E.

A text-book of surgery. New York and Phila., 1903. 8°.

BUMSTEAD, F. J.

The pathology and treatment of venereal diseases. 3. ed. Phila., 1874. 8°.

BURCKHARDT, E.

Endoskopie und endoskopische Therapie der Krankheiten der Harnröhre und Blase. Tübingen, 1889. 8°.

BURTON, R.

The anatomy of melancholy, what it is, with all the kinds, causes, symptoms, prognostics, and several cures of it. 3 vols. Boston, 1859. 12°.

CARMICHAEL, R.

An essay on the venereal diseases which have been confounded with syphilis, and the symptoms which exclusively arise from that poison. Dublin, 1814. 4°. An essay on venereal diseases, and the uses and abuses of mercury in their treatment. 2. ed. London, 1825. 8°.

* This list has been prepared in the library by Miss Minnie W. Blogg and her assistants, Miss Foster and Miss Ebaugh, whose efficient services are well known and appreciated by all connected with The Johns Hopkins Hospital and Medical School.

- CARSON, J.**
Illustrations of medical botany. The drawings on stone by J. H. Colen. 5 vols. Phila., 1847. Fol.
- CASPER, L.**
Lehrbuch der Urologie, mit Einschluss der männlichen Sexualerkrankungen. Berlin und Wien, 1903. 8°.
A text-book of genito-urinary diseases, including functional sexual disorders in man. Transl. and ed. by C. W. Bonney. Phila., 1906. 8°.
The same. 2. ed. 1909.
- CASPER, L., and LOHNSTEIN, H.**
Monatsberichte über die gesamtleistungen auf dem Gebiete der Krankheiten des Harn- und Sexual-Apparates. 4 vols. Berlin, 1896-1899. 8°.
- CASPER, L., and RICHTER, P. F.**
Functionelle Nierendiagnostik mit besonderer Berücksichtigung der Nierenchirurgie. Berlin und Wien, 1901. 8°.
- CATHELIN, F.**
Le cloisonnement vésical et la division des urines. Paris, 1903. 12°.
Conférences cliniques de chirurgie urinaire. Paris, 1909. 8°.
- CENTRALBLATT FÜR DIE KRANKHEITEN DER HARN- UND SEXUAL-ORGANE.**
Vols. 11-16, 1900-1905. Leipzig. 6 vols. 8°.
- CHESELDEN, W.**
The anatomy of the human body. 7. ed. London, 1756. 12°.
- CHEVALIER, E.**
Chirurgie des voies urinaires. Paris, 1899. 16°.
- CHEYNE, W. W., and BURGHARD, F. F.**
A manual of surgical treatment. Vol. 7. Phila. and New York. 1903. 8°.
- CHILDS, G. B.**
Gonorrhœa and its consequences; with a short historical sketch of the venereal disease. London, 1843. 12°.
- CHOPART, F.**
Traité des maladies des voies urinaires. Paris, 1841. 12°.
The same. Paris, 1855. 8°.
- CIVIALE, J.**
Nouvelles considérations sur la rétention d'urine. Paris, 1823. 8°.
Parallèle des divers moyens de traiter les calculeux. Paris, 1836. 8°.
Traité de l'affection calculeuse, ou recherches sur la formation, les caractères physiques et chimiques, les causes, les signes et les effets pathologiques de la pierre et de la gravelle [etc.]. Paris, 1838. 12°.
Traité pratique et historique de la lithotritie. Paris, 1847. 8°.
Traité pratique sur les maladies des organes génito-urinaires. 2. ed. 3 vols. Paris, 1850-1851. 12°.
The same. 3. ed. 3 vols. Paris, 1858-1860. 8°.
Collection de calculs urinaires et d'instruments de chirurgie. Paris, 1869. 8°.
La lithotritie et la taille, guide pratique pour le traitement de la pierre. Paris, 1870. 8°.
- CLARE, P.**
A new and easy method of curing the lues venerea by the introduction of mercury into the system through the orifices of the absorbent vessels on the inside of the mouth. 3. ed. London, 1780. 12°.
- CLERC, F. F.**
Traité pratique des maladies vénériennes. Vol. 1. Paris, 1866. 8°.
- COCKBURN, W.**
The symptoms, nature, cause and cure of a gonorrhœa. 3. ed. London, 1719. 12°.
- COLUMBIA UNIVERSITY, NEW YORK CITY.**
Studies from the laboratory for surgical research. Vol. 1. 1903-1907. 8°.
- CONGRÈS INTERNATIONAL DE MÉDECINE, XIII, PARIS, 1900.**
Paris-médical, assistance et enseignement, Paris, 1900. 8°.
- CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS, TRANSACTIONS.**
Vols. 6-7. 1903, 1907. 8°.
- COOPER, Sir A.**
Observations on the structure and diseases of the testis. London, 1830. Fol.
The same. 2. ed. 1841.
- COOPER, A.**
Syphilis and pseudo-syphilis. London, 1884. 8°.
- COOPER, S.**
The first lines of the practice of surgery. Phila., 1808. 8°.
- CORFE, G.**
A popular treatise on the kidney; its hitherto unknown functions and its diseases, in connection with the circulating animal oils, etc. London, 1839. 8°.
- COULSON, W.**
On the diseases of the bladder and prostate gland. 6. ed. New York, 1881. 8°.
- COUNCILMAN, W. T.**
Pathology. Boston, 1912. 8°.
- COURTENAY, F. B.**
On spermatorrhœa and certain functional derangements and debilities of the generative system: their nature, treatment and cure. 11. ed. London, 1878. 16°.
- CRILE, G. W.**
Experimental research into the surgery of the respiratory system. 2. ed. Phila., 1900. 8°.
An experimental and clinical research into certain problems relating to surgical operations. Phila., 1901. 8°.
Blood-pressure in surgery, an experimental and clinical research. Phila. and London, 1903. 8°.
- CROOKSHANK, E. M.**
Manual of bacteriology. 2. ed. London, 1887. 8°.
- CRUIKSHANK, W.**
The anatomy of the absorbing vessels of the human body. 2. ed. London, 1790. 8°.
- CRUVEILHIER, J.**
Anatomie pathologique du corps humain. 2 vols. Paris, 1829-1842. Fol.
- CULLEN, T. S.**
Cancer of the uterus, its pathology, symptomatology, diagnosis and treatment. New York, 1900. 4°.
- CULLERIER, A. P. A.**
Des affections blennorrhagiques. Paris, 1861. 8°.
- CULVERWELL, R. J.**
Medical consultations. On morbid secretions, stricture, and irritability of the urethra, etc. London, 1838. 8°.
- CURLING, T. B.**
Traité pratique des maladies du testicule, du cordon spermatique et du scrotum. Trad. de l'anglais sur la 2. éd. par L. Gosselin. Paris, 1857. 8°.
A practical treatise on the diseases of the testis and of the spermatic cord and scrotum. 3. ed. London, 1866. 8°.
- DAWSON, R.**
An essay on spermatorrhœa, and urinary deposits, with observations on the nature, causes, and treatment of the various disorders of the generative system. 5. ed. London, 1851. 12°.
The same. 6. ed. London, 1852. 12°.
- DELBET, P.**
Anatomie chirurgicale de la vessie. Paris, 1895. 8°.
Vessie, urètre, prostate, verge, périnée. Paris, 1901. 8°.
- DELEFOSSE, E.**
Pratique de la chirurgie des voies urinaires. Paris, 1878. 12°.
- DESAULT, P. J.**
Traité des maladies des voies urinaires. Paris [1799]. 12°.
- DESNOS, E., and MINET, H.**
Traité des maladies des voies urinaires. Paris, 1909. 8°.
- DEVENTER, H.**
The art of midwifery improved. Fully and plainly laying down whatever instructions are requisite to make a compleat midwife. London, 1716. 8°.
- DIONIS, P.**
Cours d'opérations de chirurgie, démontrées au Jardin Royal. 7. éd. revue, augmentée de remarques importantes par G. de la Faye. Paris, 1773. 8°.
- DISSE, J.**
Harn- und Geschlechtsorgane. I. Teil. Harnorgane. Jena, 1902. 8°.
- DOLBEAU, H. F.**
De l'épispadias ou fissure uréthrale supérieure et de son traitement. Paris, 1861. Fol.
- DOUGLAS, R.**
Surgical diseases of the abdomen. Phila., 1903. 8°.
- DUCAMP, T.**
A treatise on retention of urine, caused by structures in the urethra. Transl. from the French by W. M. Herbert. New York, 1827. 8°.
- DUPIERRIS, M.**
Mémoire sur les rétrécissements organiques du canal de l'urètre, et sur l'emploi de nouveaux instruments de scarification et d'incision pour obtenir la cure radicale de cette maladie, suivi d'un appendice sur le traitement des rétrécissements par la malaxation. Nouv. éd. Paris, 1847. 8°.
- DUPUYTREN, G.**
Mémoire sur une manière nouvelle de pratiquer l'opération de la pierre, terminé et publié par J. L. Sanson et L. J. Bégin. Paris, 1836. Fol.
- DURKEE, S.**
A treatise on gonorrhœa and syphilis. Boston, 1859. 8°.
- ENGLISCH, J.**
Ueber die neueren Behandlungsmethoden der Prostatahypertrophie. (Kastration, Ligatur des Samenstranges, Organotherapie.) Wien, 1897. 8°.
- ESBACH, G. H.**
Les calculs urinaires et biliaires; physiologie, analyse, thérapeutique. Paris, 1885. 8°.
- ESTES, W. L.**
The treatment of fractures. New York, 1900. 8°.
- FAUDACQ, C. F.**
Réflexions sur les playes, ou la méthode de procéder à leur curation [etc.]. Paris, 1736. 16°.

- FENWICK, E. H.
The electric illumination of the bladder and urethra as a means of diagnosis of obscure vesico-urethral diseases. 2. ed. London, 1889. 8°.
The value of radiography in the diagnosis and treatment of urinary stone. London, 1908. 8°.
- FERNELIUS, AMBIANUS J.
Universa medicina ab ipso quidem authore ante obitum diligenter recognita et justis accessionibus locupletata [etc.]. Editio octava. Lugduni, 1615. Fol.
- FINGER, E.
Die Syphilis und die venerischen Krankheiten. 3. Aufl. Leipzig und Wien, 1892. 8°.
Die Blennorrhöe der Sexualorgane und ihre Complicationen [etc.]. 3. Aufl. Leipzig und Wien, 1893. 8°.
- FLINT, A.
Manual of chemical examination of the urine in disease. 4. ed. New York, 1875. 12°.
The same. 5. ed. New York, 1883.
- FLUEGEL, M.
Exodus, Moses and the Decalogue legislation [etc.]. Baltimore, 1910. 8°.
- FLÜGGE, C. G. F. W.
Die Mikroorganismen, mit besonderer Berücksichtigung der Ätiologie der Infektionskrankheiten. 3. Aufl. 2 vols. Leipzig, 1896. 8°.
- FOOT, J.
Abhandlung über die Lustseuche und die Urinverhaltungen. Aus dem Englischen übersetzt von G. C. Reich. 2 vols. in 1. Leipzig, 1793-1794. 12°.
- FOUQUÉ, C.
Contribution a l'étude de la prostatectomie hypogastrique. Lyon, 1913.
- FOURNIER, A.
Leçons sur la syphilis, étudiée plus particulièrement chez la femme. Paris, 1873. 8°.
Leçons cliniques sur la syphilis, étudiée plus particulièrement chez la femme. 2. éd. Paris, 1881. 8°.
Leçons sur la syphilis tertiaire faites à l'Hôpital de Lourcine. Paris, 1875. 4°.
La syphilis du cerveau. Paris, 1879. 8°.
Prophylaxie publique de la syphilis. Paris, 1887. 8°.
Prophylaxie de la syphilis. Paris, 1903. 8°.
- FOWLER, G. R.
A treatise on appendicitis. 2. ed. Phila. and London, 1900. 8°.
- FRANK, J. P.
De curandis hominum morbis epitome, juxta ejus prælectiones in clinico Vindobonensi habitas. Lib. 4. De impetiginibus. Viennæ, 1810. 12°.
- FREDET, G. E.
De l'emploi du chloroforme dans les accouchements simples, dans les opérations obstétricales et dans l'éclampsie des femmes en couches. Paris, 1867. 8°.
- FREYER, P. J.
Clinical lectures on enlargement of the prostate. 3. ed. London, 1906.
- FÜRBRINGER, M.
Zur Entwicklung der Amphibienniere. Heidelberg, 1877. 8°.
- FÜRBRINGER, P.
Traité des maladies des organes génito-urinaires. 2 vols. Paris, 1892. 8°.
Text-book of diseases of the kidneys and genito-urinary organs. Transl. from the German by W. H. Gilbert. 2 vols. London, 1895-1898. 8°.
- FULLER, E.
Diseases of the genito-urinary system. New York, 1900. 8°.
- GANT, F. J.
The irritable bladder: its causes and curative treatment. 2. ed. London, 1867. 12°.
- GAUJOT, G., and SPILLMANN, E.
Arsenal de la chirurgie contemporaine, description, mode d'emploi et appréciation des appareils et instruments en usage pour le diagnostic, et le traitement des maladies chirurgicales. 2 vols. Paris, 1867-1872. 8°.
- GÉLY, J. A.
Études sur le cathétérisme curviligne et sur l'emploi d'une nouvelle sonde dans le cathétérisme évacuatif. Paris, 1861. 4°.
- GIORDANO, D., comp.
Trattato di chirurgia, compendio di chirurgia operatoria Italiana. Torino, 1907. 4°.
- GOLDBERG, B.
Die Verhütung der Harninfektion. Handhabung der Asepsis und Antisepsis bei der Behandlung der Harnkrankheiten. Wiesbaden, 1904. 8°.
- GRANT, H. H.
A text-book of surgical principles and surgical diseases of the face, mouth, and jaws. Phila. and London, 1902. 8°.
- GREEN, T. H.
An introduction to pathology and morbid anatomy. 6. Am. from the 7. English ed. Phila., 1889. 8°.
- GROSS, S. D.
A practical treatise on the diseases, injuries, and malformations of the urinary bladder, the prostate gland, and the urethra. 2. ed. Phila., 1855. 8°.
The same. 3. ed. Phila., 1876. 8°.
- GROSS, S. W.
A practical treatise on impotence, sterility, and allied disorders of the male sexual organs. Phila., 1881. 8°.
The same. 2. ed. Phila., 1883. 8°.
- GRÜNFELD, J.
Der Harnröhrenspiegel (das Endoskop) seine diagnostische und therapeutische Anwendung. Wien, 1877. 8°.
- GRUNER, C. G.
De morbo gallico, scriptores medici et historici partim inediti partim rari et notationibus aucti. Jena, 1793. 8°.
- GÜTERBOCK, P.
Die chirurgischen Krankheiten der Harnorgane. Vol. 4. Die chirurgischen Krankheiten der Nieren. Leipzig und Wien, 1898. 8°.
- GUIBOUT, E.
Leçons cliniques sur les maladies de la peau. Paris, 1876. 8°.
- GUTHRIE, G. J.
On the anatomy and diseases of the urinary and sexual organs. London, 1836. 8°.
- GUYON, J. C. F.
Leçons cliniques sur les affections chirurgicales de la vessie et de la prostate. Paris, 1888. 8°.
Leçons cliniques sur les maladies des voies urinaires. 3. ed. 2 vols. Paris, 1894-1896. 8°.
- GUYON, J. C. F., and BAZY, P.
Atlas des maladies des voies urinaires. Maladies de l'urèthre et de la prostate. Paris, 1886. 8°.
- HALLÉ, N.
Urétérites et pyélites. Paris, 1887. 8°.
- HAMDY, I.
De la circoncision. Montpellier, 1873. 8°.
- HANDBUCH DER UROLOGIE.
Vol. 2, 1905. Wien. 8°.
- HARRISON, J.
The pathology and treatment of venereal diseases. London, 1860. 8°.
- HARRISON, R.
Clinical lectures on stricture of the urethra and other disorders of the urinary organs. London and Liverpool, 1878. 8°.
- HARTMANN, H.
Des névralgies vésicales. Paris, 1889. 8°.
Organes génito-urinaires de l'homme. Paris, 1904. 4°.
- HAUGHTON, S.
A manual of optics. New York, 1899. 16°.
- HAYDEN, J. R.
Venereal diseases. 3. ed. Phila. and New York, 1901. 12°.
- HEATH, C.
A course of operative surgery, with plates drawn from nature by M. Léveillé. Phila., 1878. 4°.
- HEITZMANN, C.
Anatomy, descriptive and topographical. English ed. by L. Heitzmann. New York, 1887. 8°.
- HELVETIUS, A.
Traité des maladies les plus fréquentes et des remèdes propres à les guérir. 3. éd. Paris, 1724. 16°.
- HENRY, M. H.
The treatment of venereal diseases; a monograph on the method pursued in the Vienna hospital. Adapted and arranged from the German. New York, 1872. 8°.
- HEURTELOUP, C. L. S.
De la lithotripsie sans fragments au moyen des deux procédés de l'extraction immédiate. Paris, 1846. 8°.
Rétrécissements, de l'urètre. Guérisons immédiates, permanentes, authentiques et nombreuses [etc.]. 2. ed. Paris, 1859. 8°.
- HIND, G. W.
A series of twenty plates illustrating the causes of displacement in the various fractures of the bones of the extremities. 2. ed. London, 1836. Fol.
- HOFFMAN, K. B., and ULTMANN, R.
Guide to the examination of urine, with special reference to the diseases of the urinary apparatus. 2. ed. Transl. and ed. by F. Forchheimer. Cincinnati, 1886. 12°.
- HOLMES, B.
Surgery of the head. New York, 1903. 8°.
- HOME, Sir E.
Practical observations on the treatment of strictures in the urethra and in the œsophagus. Vol. 2. London, 1803. 8°.
Practical observations on the treatment of the diseases of the prostate gland. Illustrated by copper plates. 2 vols. London, 1811-1818.
- HOPKINS, W. B.
A clinical treatise on fractures. Phila., 1900. 8°.
- HOBION, C.
Des rétentions d'urine ou pathologie spéciale des organes urinaux au point de vue de la rétention. Paris, 1863. 8°.

HOWSHIP, J.

Practical observations on the diseases of the urinary organs. London, 1816. 8°.
A practical treatise on the symptoms, causes, discrimination, and treatment of some of the most important complaints that affect the secretion and excretion of the urine. London, 1823. 8°.

HUNTER, J.

A treatise on the venereal disease. 1. ed. London, 1786. 4°.
The same. 2. ed. London, 1787. 4°.
A treatise on the venereal disease. With an introduction and commentary by J. Adams. London, 1810. 8°.
The same. 3. ed. Enlarged from the materials left by the author for that purpose; with occasional observations of the editor, Everard Home. London, 1810. 4°.
The same. First Am. ed. Phila., 1818. 8°.
The same. With an introduction and commentary by J. Adams. 2. ed. London, 1818. 8°.
The same. With copious additions by Dr. P. Ricord. Ed. by F. J. Bumstead. Phila., 1853. 8°.

HYDE, J. N., and MONTGOMERY, F. H.

A manual of syphilis and the venereal diseases. 2. ed. Phila., 1900. 8°.

INTERNATIONALES CENTRALBLATT FÜR DIE PHYSIOLOGIE UND PATHOLOGIE DER HARN- UND SEXUAL-ORGANE.

Vols. 1-10, 1889-1899. Hamburg and Leipzig. 10 vols. 8°.

ISRAEL, J.

Chirurgische Klinik der Nierenkrankheiten. Berlin, 1901. 8°.

JACOBS, P. P., comp.

A tuberculosis directory. New York, 1911. 8°.

JACOBSON, W. H. A.

The operations of surgery. Phila., 1889. 8°.

JACOBY, S.

Lehrbuch der Kystoskopie und stereokystographischer Atlas. Leipzig, 1911. Fol.

JARJAVAY, J. F.

Recherches anatomiques sur l'urètre de l'homme. Paris, 1856. 4°.

JEANCON, J. A.

Diseases of the sexual organs. Cincinnati, 1891. Fol.

JOHNS HOPKINS HOSPITAL REPORTS.

Vol. 13, 1906, 1 copy; vol. 14, 1906, 4 copies. Baltimore. 5 vols. 4°.

JORES, L.

Harnorgane [and other articles, reprinted from Ergebnisse der allgemeinen Pathologie und pathologischen Anatomie des Menschen und der Tiere]. Wiesbaden, 1898. 8°.

JULLIEN, L.

Traité pratique des maladies vénériennes. Paris, 1879. 8°.

KAPOSI, M.

Pathologie und Therapie der Syphilis. Stuttgart, 1891. 8°.

KAUFMANN, C.

Verletzungen und Krankheiten der männlichen Harnröhre und des Penis. Stuttgart, 1886. 8°.

KAULA, H.

De la Spermatorrhée. Paris, 1846. 4°.

KEEGAN, D. F.

Litholapaxy in male children and male adults. London, 1887. 8°.

KEEN, W. W., and WHITE, J. W., eds.

An American text-book of surgery. 3. ed. Phila., 1899. 8°.

KEHR, H.

Introduction to the differential diagnosis of the separate forms of gall-stone disease. Transl. by W. W. Seymour. Phila., 1901. 8°.

KEY, C. A.

A short treatise on the section of the prostate gland in lithotomy. London, 1824. 4°.

KEY, G.

Remarks on the observations of Mr. Gataker on venereal complaints. London, 1755. 12°.

KEYES, E. L.

The surgical diseases of the genito-urinary organs, including syphilis. New York, 1892. 8°.

KEYES, E. L., and CHETWOOD, C. H.

Venereal diseases. New York, 1900. 8°.

KING, W. H.

Electricity in medicine and surgery. 2. ed. New York, 1902. 8°.

KLEMPERER, F., and LEVY, E.

Grundriss der klinischen Bakteriologie. Berlin, 1894. 8°.

KNOPF, S. A.

Tuberculosis as a disease of the masses and how to combat it. 5. ed. New York, 1908. 8°.

KOENIG, A.

Die neueren Hilfsmittel zur Diagnose und Therapie der Blasenkrankheiten. Leipzig [n. d.]. 12°.

KÖHN, E.

Die Syphilis während der Periode ihrer Initial- und Frühformen und deren Behandlung. Auf grund von Fournier's "Leçons sur la syphilis." Wien, 1875. 8°.

VON KRAFFT-EBING, R.

Psychopathia sexualis mit besonderer Berücksichtigung der conträren Sexualempfindung. 6. Aufl. Stuttgart, 1891. 8°.

LAFFECTEUR, D.

Traité des maladies vénériennes anciennes, récentes, occultes ou dégénérées, et méthode de leur guérison par le rob anti-syphilitique. Paris, 1807. 8°.

LALLEMAND, C. F.

On the causes, symptoms, and treatment of spermatorrhœa. Transl. and ed. by H. J. McDougall. 2. ed. London, 1851. 8°.
The same. 5. Am. ed. Phila., 1866. 8°.

LANE, J. R.

Lectures on syphilis; delivered at the Harveian Society, December, 1876. 2. ed. London, 1881. 12°.

LANG, E.

Vorlesungen über Pathologie und Therapie der venerischen Krankheiten. 2. Theil, 1. Hft. Das venerische Geschwür. Wiesbaden, 1887. 8°.

LANZ, A.

Klinische und experimentelle Beiträge zur Pathogenese der mercuriellen Stomatitis und Salivation. Berlin, 1897. 8°.

LARREY, D. J.

Memoirs of military surgery, and campaigns of the French armies on the Rhine, in Corsica, Catalonia, Egypt, and Syria; at Boulogne, Ulm, and Austerlitz; in Saxony, Prussia, Poland, Spain and Austria. From the French by R. W. Hall. 1. Am. from the 2. Par. ed. 2 vols. Baltimore, 1814. 8°.

LEDOUBLE, A.

De l'épididymite blennorrhagique. Tours, 1878. 8°.

LEE, H.

Lectures on syphilis. Phila., 1875. 8°.
Lectures on syphilis and on some forms of local disease. London, 1875. 8°.

LEROY-D'ÉTIOLLES, J. J. J.

Exposé des divers procédés employés jusqu'à ce jour pour guérir de la pierre, sans avoir recours à l'opération de la taille. Paris, 1825. 8°.
De la lithotripsie. Mémoire no. 1. Paris, 1836. 12°.
Urologie. Des angusties ou rétrécissements de l'urètre et de leur traitement rationnel. Paris, 1845. 8°.

LEROY-D'ÉTIOLLES, R. H., FILS.

Traité pratique de la gravelle et des calculs urinaires. Paris, 1866. 8°.
The same. 2. éd. Paris, 1869. 8°.

LESSER, E.

Lehrbuch der Haut- und Geschlechtskrankheiten. Vol. 1, 11. ed. Vol. 2, 12. ed. 2 vols. Leipzig, 1904-1906. 8°.

LISTER, Lord.

The third Huxley lecture delivered before the medical school of Charing Cross Hospital on October 2, 1900. (Revised, 1907.) London, 1907.

LITTLE, S. W.

Nephritis. New York, 1907. 12°.

LOEBISCH, W. F.

Anleitung zur Harn-Analyse. Wien, 1878. 8°.

LUGOL, J. G. A.

Researches on scrofulous diseases. Transl. from the French by A. S. Doane. New York, 1845. 12°.

LUSK, W. T.

The science and art of midwifery. New York, 1893. 8°.

LUYS, G.

La séparation d'urine des deux reins. Paris, 1904. 8°.

MALGAIGNE, J. F.

Manuel de médecine opératoire fondée sur l'anatomie normale et l'anatomie pathologique. 3. éd. Paris, 1840. 16°.
Traité des fractures et des luxations. 2 vols. Paris, 1847-1855. 8°.

MARAT, J. P.

Reprint of two tracts. I. An essay on gleet. II. An enquiry into the nature, cause and cure of a singular disease of the eyes. Ed. with an introd. by J. B. Bailey. London, 1891. 8°.

MARCET, A.

Essai sur l'histoire chimique des calculs et sur le traitement médical des affections calculeuses. Trad. de l'anglais sur la 2. éd. par J. Riffault. Paris, 1823. 8°.

MARTENS, M. A. H.

Die Verletzungen und Verengerungen der Harnröhre und ihre Behandlung. Berlin, 1902. 8°.

MASSEY, G. B.

Conservative Gynecology and Electro-therapeutics. 3. ed. Phila., 1898. 8°.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, TRANSACTIONS.

1905.

MÉMOIRES DE L'ACADÉMIE ROYALE DE CHIRURGIE.

Vols. 2, 3, 6-15, 1771-1774. Paris. 12 vols. 16°.

- MERCIER, L. A.
Recherches anatomiques, pathologiques et thérapeutiques sur les maladies des organes urinaux et génitaux considérées spécialement chez les hommes âgés. Paris, 1841. 8°.
Recherches sur la nature et le traitement d'une cause fréquente et peu connue de rétention d'urine. Paris, 1844. 8°.
Recherches anatomiques, pathologiques et thérapeutiques sur les valvules du col de la vessie cause fréquente et peu connue de rétention d'urine. 2. éd. Paris, 1848. 8°.
Recherches sur le traitement des maladies des organes urinaux. Paris, 1856. 8°.
- MILTON, J. L.
On a new way of treating gonorrhœa. London, 1852. 8°.
On the pathology and treatment of spermatorrhœa. 12. ed. London, 1887. 8°.
- MINOT.
De la nature et des causes de la fièvre; du légitime usage de la saignée et des purgatifs. 2. éd. Paris, 1691. 16°.
- MITCHELL, C.
A clinical study of diseases of the kidney. Chicago, 1890. 8°.
- MONATSBERICHTE FÜR UROLOGIE.
Vols. 6-11, 1901-1906. Berlin. 6 vols. 8°.
- MONOD, C. E., and TERRILLON, O.
Traité des maladies du testicule et de ses annexes. Paris, 1889. 8°.
- MORLAND, W. W.
Diseases of the urinary organs. Phila., 1858. 8°.
- MORRIS, H.
Surgical diseases of the kidney. Phila. [1885]. 16°.
- MORROW, P. A., ed.
A system of genito-urinary diseases, syphilology and dermatology by various authors. 3 vols. New York, 1893-1894. 8°.
- MORTON, H. H.
Genito-urinary diseases and syphilis. Phila., 1902. 8°.
The same. 2. ed. 1906.
The same. 3. ed. 1912.
- MRACEK, F.
Atlas of syphilis and the venereal diseases. Transl. from the German by L. B. Bangs. Phila., 1898. 12°.
- MUMFORD, J. G.
A narrative of medicine in America. Phila. and London, 1903. 8°.
- MUNDÉ, P. F.
Minor surgical gynecology. 2. ed. New York, 1885. 8°.
- MYNTER, H.
Appendicitis and its surgical treatment. 3. ed. Phila., 1900. 8°.
- NAPHEYS, G. H.
Modern therapeutics, medical and surgical, including the diseases of women and children. 9. ed. 2 vols. Phila., 1892-1893. 8°.
- NELIGAN, J. M.
Atlas of cutaneous diseases. Phila., 1867. 4°.
- NEWMAN, D.
Lectures to practitioners. On the diseases of the kidney amenable to surgical treatment. London, 1888. 8°.
Movable kidney and other displacements and malformations. London, 1907. 8°.
- NEW YORK STATE, WATER SUPPLY COMMISSION.
Annual report, Vol. 5, 1910. Albany. 8°.
- OBERLÄNDER, F. M.
Lehrbuch der Urethroskopie. Leipzig, 1893. 8°.
Die chronische Gonorrhœ der männlichen Harnröhre. Leipzig, 1901. 8°.
- OBERLÄNDER, F. M., and KOLLMANN, A.
Die chronische Gonorrhœ der männlichen Harnröhre und ihre Komplikationen. 2. Aufl. Leipzig, 1910. 8°.
- OCHSNER, A. J., and THOMPSON, R. L.
The surgery and pathology of the thyroid and parathyroid glands. St. Louis, 1910. 8°.
- OPPENHEIMER, R.
Urologische Operationslehre. Wiesbaden, 1910. 4°.
- ORTH, J.
Lehrbuch der speciellen pathologischen Anatomie. Bd. 2. Berlin, 1889. 8°.
- OSLER, Sir W., and McCRAE, T., eds.
Modern medicine: its theory and practice. Vols. 2, 3, 5. Phila. and New York, 1914-1915. 8°.
- OTIS, F. N.
Stricture of the male urethra; its radical cure. New York, 1878. 8°.
The same. [2. ed.] New York, 1880.
- OVERALL, G. W.
A non-surgical treatise on diseases of the prostate gland and adnexa. Chicago, 1903. 12°.
- PAGET, Sir J.
Descriptive catalogue of the pathological specimens contained in the museum of the Royal College of Surgeons of England. 2. ed. London, 1885. 8°.
- PAPIN, E.
Les fonctions sexuelles et la prostatectomie. Paris, 1908. 8°.
Manuel de cystoscopie. Paris, 1914. 8°.
- PARK, R., ed.
A treatise on surgery by American authors. 2 vols. Phila. and New York, 1896. 8°.
- PASTEAU, O.
État du système lymphatique dans les maladies de la vessie et de la prostate. Paris, 1898. 8°.
- PEARSON, J.
Observations on the effects of various articles of the materia medica in the cure of lues venerea. London, 1807. 8°.
- PECHEY, J.
A collection of chronical diseases. London, 1692. 16°.
- PEISSE, J. L. H.
Sketches of the character and writings of eminent living surgeons and physicians of Paris. Transl. from the French by Elisha Bartlett. Boston, 1831. 8°.
- PERRÈVE, P. E. W. V.
Traité des rétrécissements organiques de l'urètre. Paris, 1847. 8°.
- PETIT, J.
De la prostatectomie périnéale dans l'hypertrophie simple de la prostate. Paris, 1902. 8°.
- PETIT, J. L.
Traité des maladies des os; dans lequel on a représenté les appareils et les machines qui conviennent à leur guérison. 3. éd. Vol. 1. Paris, 1736. 16°.
- PICK, T. P.
Surgery. London, 1899. 8°.
- PINKUS, F.
Haut- und Geschlechts-Krankheiten. Leipzig, 1910. 8°.
- POIRIER, P., and CHARPY, A., eds.
Traité d'anatomie humaine. Vol. 5. Paris, 1904. 4°.
- POUSSON, A.
Conférences sur les maladies de la prostate, des urètres et des reins. [n. d.] 8°.
- PROUST, R.
De la prostatectomie périnéale totale. Paris, 1900. 8°.
Manuel de la prostatectomie périnéale pour hypertrophie. Paris, 1903. 8°.
La prostatectomie dans l'hypertrophie de la prostate. Paris, 1904. 4°.
- PURDY, C. W.
Practical urinalysis and urinary diagnosis. 4. ed. Phila. and New York, 1899. 8°.
- QUAIN, J.
Elements of anatomy. 9. ed. 2 vols. New York, 1882. 8°.
- RALFE, C. H.
A practical treatise on diseases of the kidneys and urinary derangements. Phila., 1885. 12°.
- RAMSDEN, T.
Practical observations on the sclerocele and other morbid enlargements of the testicle. London, 1811. 8°.
- RECLUS, P.
Du tubercule du testicule et de l'orchite tuberculeuse. Paris, 1876. 8°.
De la syphilis du testicule. Paris, 1882. 8°.
- REES, G.
A treatise on the primary symptoms of lues venerea with a concise critical and chronological account of all the English writers on this subject from the year 1735 (being the period at which Dr. Astruc concluded his historical account) to 1785. London, 1802. 8°.
- RELIGUET, E.
Traité des opérations des voies urinales. Paris, 1869-1870. 8°.
- REMONDINO, P. C.
History of circumcision from the earliest times to the present. Phila. and London, 1891. 12°.
- RETZIUS, M. G.
Biologische Untersuchungen. Neue Folge, vol. 5, 1893; vol. 11, 1904; vol. 13, 1906; vol. 14, 1909. (4 parts.)
- REYBARD, J. F.
Traité pratique des rétrécissements du canal de l'urètre. Paris, 1853. 8°.
- REYNAUD, A. A. M.
Traité pratique des maladies vénériennes. Toulon and Paris, 1845. 8°.
- RICKETSON, S.
Means of preserving health and preventing diseases. New York, 1806. 16°.
- RICKETTS, B. M.
The surgery of the heart and lungs. New York, 1904. 8°.
Surgery of the prostate, pancreas, diaphragm, spleen, thyroid, and hydrocephalus. A historical review. Cincinnati, 1904. 4°.

RICORD, P.

Lectures on venereal and other diseases. Phila., 1849. 12°.
 Illustrations of syphilitic disease. Transl. from the French by T. F. Betton: with the addition of a history of syphilis, and a complete bibliography and formulary of remedies, by P. B. Goddard. Phila., 1851. 8°.
 Letters on syphilis. Transl. by W. P. Lattimore. Phila., 1852. 8°.
 A practical treatise on venereal diseases; or, critical and experimental researches on inoculation. Transl. from the French by A. S. Doane. 13. ed. Redfield, 1854.
 Leçons sur le chancre. 2. éd. Paris, 1860. 8°.

RINGLEB, O.

Das Kystoskop. Leipzig, 1910. 8°.

ROBERTS, J. B.

A manual of modern surgery. Phila., 1890. 8°.

ROBERTS, W.

A practical treatise on urinary and renal diseases. 4. ed. Phila., 1885. 8°.

ROBINSON, N.

A compleat treatise of the gravel and stone. 3. ed. London, 1734. 8°.

ROHÉ, G. H.

Text-book of hygiene. 2. ed. Phila. and London, 1890. 8°.

ROHRER, C. F.

Das primäre Nierencarcinom. Zürich, 1874. 8°.

ROSENSTEIN, S. S.

Die Pathologie und Therapie der Nierenkrankheiten. 4. Aufl. Berlin, 1894. 8°.

DE ROUVILLE, G.

Consultations sur les maladies des voies urinaires à l'usage des praticiens. Paris, 1903. 8°.

ROVSING, T.

Klinische und experimentelle Untersuchungen über die infektiösen Krankheiten der Harnorgane. Berlin, 1898. 8°.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.

A descriptive and illustrated catalogue of the calculi and other animal concretions contained in the museum of the Royal College of Surgeons in London. 1842-1845. Supplement I, by Thomas Taylor. London, 1871. 3 vols. 4°.

RUMPEL, O.

Die Cystoskopie im Dienste der Chirurgie. Berlin und Wien, 1909. 8°.

SAVAGE, H.

The surgery, surgical pathology, and surgical anatomy of the female pelvic organs. 2. ed. London, 1870. Fol.

SCHEDE, M.

Meine Erfahrungen über Nierenexstirpationen. Hamburg, 1889. 4°.

SCHLAGINTWEIT, F.

Prostatahypertrophie und Bottinische Operation. Leipzig, 1902. 8°.

SCHLEISS VON LÖWENFELD, M. J.

Die Lithotripsie in Bezug auf Geschichte, Theorie und Praxis derselben unter Benützung der neuesten Erfahrungen der französischen Aerzte hierüber. München, 1839. 8°.

SCUDDER, C. L.

The treatment of fractures. 4. ed. Phila., New York and London, 1903. 8°.

SÉGALAS, P. S.

Essai sur la gravelle et la pierre, considérées sous le rapport de leurs causes, de leurs effets, et de leurs divers modes de traitement. Atlas. Paris, 1839. Fol.

SENATOR, H.

Die Erkrankungen der Nieren. Wien, 1896. 8°.

SENN, N.

Principles of surgery. Phila. and London, 1890. 8°.
 Tuberculosis of the genito-urinary organs, male and female. Phila., 1897. 8°.
 The pathology and surgical treatment of tumors. 2. ed. Phila., 1900. 8°.

SIMON, F. A.

Pseudomessias syphiliticus. Antwortschreiben auf Ricord's Briefe über Syphilis. Hamburg, 1852. 8°.

SIMON, G.

Chirurgie der Nieren. 2 parts in 1 vol. Pt. 1. Erlangen, 1871. Pt. 2. Stuttgart, 1876. 8°.

SIMPSON, Sir J. Y.

Anæsthesia, or the employment of chloroform and ether in surgery, midwifery, etc. Phila., 1849. 8°.

SKEY, F. C.

A practical treatise on the venereal disease. London, 1840. 12°.

SMELLIE, W.

A set of anatomical tables, with explanations, and an abridgment of the practice of midwifery. First Worcester ed. Worcester, Mass., 1793. 8°.

SMITH, N.

Medical and surgical memoirs. Ed. by N. R. Smith. Baltimore, 1831. 8°.

SMITH, N. R.

Surgical anatomy of the arteries. Baltimore, 1830. 4°.

SMITH, S.

Manual of the principles and practice of operative surgery. Boston, 1880. 12°.

SOUTHERN SURGICAL AND GYNECOLOGICAL ASSOCIATION, TRANSACTIONS.

Vols. 13-19, 1900-1906; vols. 21-27, 1908-1914. 14 vols. 8°.

SQUIER, J. B., and BUGBEE, H. G.

Manual of cystoscopy. New York, 1911. 12°.

STEIN, A. W.

A study of the tumors of the bladder, with original contributions and drawings. New York, 1881. 8°.

STERLING, J. W., tr.

Report of the Royal Academy of Medicine to the minister of the interior, upon the cholera-morbus. Published by order of the French Government. New York, 1832. 12°.

STEWART, F. C.

The hospitals and surgeons of Paris. An historical and statistical account of the civil hospitals of Paris; with miscellaneous information. New York, 1843. 8°.

STEWART, R. W.

The diseases of the male urethra. New York, 1896. 8°.

STILES, H. R.

Bundling; its origin, progress and decline in America. Albany, 1871. 12°.

STIMSON, L. A.

A practical treatise on fractures and dislocations. 3. ed. New York and Phila., 1900. 8°.

STURGIS, F. R.

The students' manual of venereal diseases. 7. ed. Phila., 1901. 8°.

SULTAN, G.

Atlas and epitome of abdominal hernias. Phila. and London, 1902. 12°.

SWEDIAUR, F.

Practical observations on venereal complaints. 3. ed. Edinburgh, 1787. 12°.
 The same. 3. ed. New York, 1788. 12°.
 Traité complet sur les symptômes, les effets, la nature et le traitement des maladies syphilitiques. 2 vols. Paris, 1801. 8°.

SYMONDS, J. A.

A problem in modern ethics; being an inquiry into the phenomenon of sexual inversion. London, 1896. 8°.
 A problem in Greek ethics; being an inquiry into the phenomenon of sexual inversion. London, 1901. 8°.

SYPHILIS.

A symposium by Bulkley, Cabot, Gwyn [et al.]. New York, 1902. 12°.

TAYLOR, R. W.

A practical treatise on genito-urinary and venereal diseases and syphilis. 2. ed. New York and Phila., 1900. 8°.
 The same. 3. ed. 1904.

TESTUT, J. L.

Traité d'anatomie humaine. 5. ed. Vol. 4. Paris, 1905. 4°.

THOMPSON, Sir H.

The pathology and treatment of stricture of the urethra, and urinary fistulae. 2. ed. London, 1858. 8°.
 The same. 3. ed. London, 1869. 8°.
 The same. 4. ed. London, 1885. 8°.
 The diseases of the prostate, their pathology and treatment. London, 1861. 8°.
 The same. 3. ed. London, 1868. 8°.
 The same. 6. ed. London, 1886. 8°.
 Clinical lectures on diseases of the urinary organs. 2. ed. London, 1869. 12°.
 The same. 2. Am. from the 3. English ed. Phila., 1874. 8°.
 The same. 4. ed. London, 1876. 8°.
 The same. 5. ed. London, 1879. 8°.
 The same. 6. ed. London, 1882. 8°.
 The same. 7. ed. London, 1883. 8°.
 The same. 8. ed. London, 1888. 8°.
 Traité pratique des maladies des voies urinaires. Paris, 1874. 8°.
 Practical lithotomy and lithotripsy, or an inquiry into the best modes of removing stone from the bladder. 3. ed. London, 1880. 8°.
 On tumours of the bladder; their nature, symptoms, and surgical treatment. London, 1884. 8°.
 On the suprapubic operation of opening the bladder for the stone and for tumours. London, 1886. 8°.

THORNTON, J. K.

The surgery of the kidneys. London, 1890. 8°.

TISSOT, S. A.

A treatise on the diseases produced by onanism. Transl. from a new ed. of the French, with notes and an appendix. New York, 1832. 12°.

TODD, R. B.

Clinical lectures on certain diseases of the urinary organs, and on dropsies. Phila., 1857. 8°.

TORRES, M.

Des calculs du rein et de la néphrotomie. Paris, 1878. 8°.

TRALL, R. T.

Pathology of the reproductive organs. Boston, 1862. 8°.
 Sexual physiology and hygiene. London, 1913. 12°.

ULTZMANN, R.

Die Harnconcretionen des Menschen und die Ursachen ihrer Entstehung. Wien, 1882. 4°.
 Pyuria; or, pus in the urine, and its treatment. Transl. by W. B. Platt. New York, 1884. 12°.
 Vorlesungen über Krankheiten der Harnorgane. Mitgeteilt und bearbeitet von Dr. J. H. Brik. Wien und Leipzig, 1892. 8°.
 The neuroses of the genito-urinary system in the male, with sterility and impotence. Transl. by G. W. Allen. Phila., 1896. 12°.

UNITED STATES CONGRESS. HOUSE OF REPRESENTATIVES.

William T. G. Morton. Sulphuric ether. Report by Dr. Edwards. Washington, 1849. 8°.

UNITED STATES. WAR DEPARTMENT.

The medical and surgical history of the war of the rebellion. Part II. Vol. II. Surgical history. Washington, 1876. Fol.

UROLOGISCHER JAHRESBERICHT, EINSCHLIESSLICH DER ERKRANKUNGEN DES MÄNNLICHEN GENITALAPPARATES.

Hrsg. von R. du Bois-Reymond, C. Bruni [et al.], 1911 and 1913. Leipzig, 1912 and 1914. 2 vols. 8°.

VALENTINE, F. C.

The irrigation treatment of gonorrhœa. New York, 1900. 8°.

VELPEAU, A. A. L. M.

Nouveaux éléments de médecine opératoire. Paris, 1832. 4°.

VERDIER, C.

Abrégé de l'anatomie du corps humain. 4. éd. 2 vols. Paris, 1768. 8°.

VICARY, T.

The Englishmans treasure; with the true anatomie of mans body . . . and now ninthly much augmented, corrected and enlarged. London, 1641. 12°.

VIDAL, de Cassis, A. T.

A treatise on venereal diseases. 3. ed. Transl. by G. C. Blackman. New York, 1865. 8°.

VIRCHOW, R. L. K.

Post-mortem examinations, with especial reference to medico-legal practice. Second Am. from the fourth German ed. Transl. by T. P. Smith. Phila., 1887. 12°.

WADD, W.

Cases of diseased bladder and testicle. Illustrated with etchings. London, 1815. 4°.

WALL, J.

Plain directions, &c., for the cure of the venereal disease. London, 1764. 8°.

WALLACE, W.

A treatise on the venereal disease and its varieties. London, 1838. 8°.

WALTER, F. A.

Recherches sur quelques maladies des reins et de la vessie urinaire, confirmées par des obductions. [Bruxelles, 1792.] 4°.

WASSERMANN, M.

Epithéliome primitif de l'urèthre. Paris, 1895. 8°.

WATSON, F. S., and CUNNINGHAM, J. H.

Diseases and surgery of the genito-urinary system. Vol. 1. Phila. and New York, 1908. 4°.

WHITE, J. W., and MARTIN, E.

Genito-urinary surgery. 9. ed. Phila. and London, 1910. 8°.

WILLSON, R. N.

The education of the young in sex hygiene. Phila., 1913. 8°.

WOSSIDLO, H.

Die Stricturen der Harnröhre und ihre Behandlung. Leipzig [n. d.]. 16°.
 Die Gonorrhœ des Mannes und ihre Komplikationen. Berlin, 1903. 8°.

WYETH, J. A.

A text-book on surgery, general, operative and mechanical. 2. ed. New York, 1893. 4°.

YOUNG, H. H.

Conservative perineal prostatectomy. Part II. In: Stereo-Clinic, Sect. xii, 44 stereos. Troy, N. Y., 1910. 4°.

ZEISSL, H.

Lehrbuch der Syphilis und der mit dieser verwandten örtlichen venerischen Krankheiten. 3. Aufl. Stuttgart, 1875. 8°.
 Lehrbuch der Syphilis. Chromolithographische Tafeln Grösstentheils nach Eigenen Original-Zeichnungenlithographiet von Dr. Julius Heitzmann. Stuttgart, 1875. 8°.

ZIEGLER, E.

Lehrbuch der speciellen pathologischen Anatomie. 7. Aufl. Vol. 2. Jena, 1892. 8°.
 Lehrbuch der allgemeinen Pathologie und der pathologischen Anatomie. 8. Aufl. Vol. 1. Jena, 1895. 8°.

ZONDEK, M.

Die Topographie der Niere und ihre Bedeutung für die Nieren-Chirurgie. Berlin, 1903. 8°.

ZUCKERKANDL, O.

Die localen Erkrankungen der Harnblase. Wien, 1899. 8°.
 Atlas und Grundriss der chirurgischen Operationslehre. 4. Aufl. München, 1909. 12°.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

FEBRUARY 5, 1917.

1. The Effect of Unilateral Excision of the Adrenal, Section of the Splanchnic and Section of the Renal Nerves, on the Secretion of the Kidney. (Abstract.) E. K. MARSHALL, JR., and A. C. KOLLS.

This work was undertaken to study the effect of unilateral excision of the adrenal on the function of the kidney of the side operated upon. Dogs were used exclusively. Paraldehyde was used as an anesthetic except in cases of survival operations which were performed aseptically under ether. The urine was collected separately from each kidney by cannulating the ureters. The amount, specific gravity, chlorides, urea and creatinine of the urine were determined on each side during one-hour periods with and without diuresis. The excretion of phenolsulphonephthalein was determined on the two sides for one hour.

The results were as follows: The excretion of the kidney on the side operated upon as compared with that of the other kidney showed: increase of water, decreased specific gravity, relative decrease but absolute increase of urea, relative and absolute increase of chlorides, relative decrease but no absolute change in creatinine and phthalein. Removal of the adrenal in the dog is necessarily associated with injury to the splanchnic. Section of the splanchnic produces the same results as removal of the adrenal. However, this does not prove that the adrenal is not concerned, for one may argue that after splanchnotomy the adrenal ceases to secrete. Section of the renal nerves without disturbance of the relations of the adrenal and kidney causes the same changes as removal of the adrenal or as section of the splanchnic nerve.

The conclusion, therefore, seems justified that the changes are brought about by injury to the splanchnic nerve.

Some of the results are interesting in themselves. We can divide the substances excreted by the kidney into two classes: (1) Those that are excreted in increased amount after nerve section, namely, water, chlorides and urea; (2) Those whose excretion is unaffected by section of the splanchnic, namely, phthalein and creatinine.

Decreasing the blood flow of one kidney by careful compression of the renal artery causes: (1) In a normal animal a decrease of water, a relative and an absolute decrease of chlorides, a relative increase and an absolute decrease in urea, a relative increase but no absolute change in phthalein and creatinine; (2) In an animal operated upon, a return of the excretion of the kidney operated upon to one approximating the normal excretion in water, chlorides, urea and creatinine. Therefore, since the same changes can be produced by altering the blood flow through the kidney as are evident after nerve section, one must conclude that the phenomena obtained after splanchnic section are caused in part, if not entirely, by vasomotor disturbances and a consequent increased blood flow through the kidney of the side operated upon.

The results which have been given above have been obtained with hypertonic sodium chloride as the diuretic. A different picture is obtained when certain other diuretics are used. If after unilateral splanchnic section one employs sodium sulphate, sodium nitrate or urea in hypertonic solution as a diuretic, the differences in the excretion of the two kidneys are absent or much less marked than without diuresis, or with sodium chloride diuresis.

2. Experiences with Acoustic Tumors. (Abstract.) DR. HARVEY CUSHING.

This was a report of some detailed studies of a series of 30 tumors of the nervus acusticus, usually incorporated in the group of so-called "cerebellopontile" tumors. In the series of 468

verified cases in the speaker's series, 8 per cent proved to be isolated tumors (neurofibromas) of the acoustic nerve. A historical summary of the past observations on these tumors was given with special reference to Cruveilhier's notable case.

The symptomatology of the tumors was described and emphasis was laid upon the importance of securing an exact chronology of the symptoms, for the majority of cases show inaugural symptoms referable to the 8th nerve. Attention was also called to the question of the Bárány reactions and of the changes in the temporal bone shown by roentgenological studies.

Chief stress was laid upon the peculiar and destructive pathological character of the tumors, which have been variously designated as endotheliomas or fibromas or gliomas, but which probably come from some congenital *Anlage* in the peripheral end of the acoustic nerve at its entrance into the internal auditory meatus. It is safe at present merely to designate them as acoustic tumors.

The operative features of these cases were described, and the speaker gave in some detail his preferential procedure with a bilateral exposure of the cerebellum and an extracerebellar approach to the tumor. The mortality of these operations in the past has been regarded as nearly 70 per cent, but in the series of operations which were reported it was much lower, about 12 per cent, owing to the fact that an intracapsular enucleation of the growth was performed rather than an attempted total extirpation.

DISCUSSION.

DR. WELCH: I agree with Dr. Cushing that the pathological side is one of the most interesting aspects of his paper, and I think it is a contribution of the first rank. These tumors are presumably tumors which correspond to growths which in the ordinary peripheral nerves are variously called neurofibromata, false neurofibromata, pseudo-neurofibromata etc., but after all essentially very much the same *Anlage*. It is the determination of this which is the capital point to my mind that comes out from Dr. Cushing's paper. It seems at first glance very disturbing to have these various names, fibroma, fibro-sarcoma, endothelioma, etc. It seems that if one pathologist calls a tumor an endothelioma and another calls it a fibro-sarcoma, they are miles apart. It is a matter of trifling importance. I do not think this great variety of designation is a matter for very severe criticism. I judge that these cases described by Dr. Cushing are not true neuromata in any sense; indeed I think the name neuroma is somewhat objectionable, although rather an old name. As I said before, these tumors evidently belong in the same category as those loosely called neuromata, pseudo-neuromata etc., in the peripheral nerves. Dr. Cushing has thrown great light upon this subject to-night.

DR. HALSTED. (Abstract.): The most interesting part I think of this paper is that one can take out these tumors with practically no mortality. In Germany the most recent statistics (as late as 1915) give a mortality of from 75 to 80 per cent, and one surgeon had a mortality of 100 per cent with quite a large number of tumors. All this is particularly interesting to one who has watched the development of the surgery of the brain. The greatest exponent in our times, next to Dr. Cushing, was Dr. Horsley, a brilliant man and a very skillful operator.

These cases that Dr. Cushing has shown are all of large tumors. They are, of course, much the most interesting to show, but I should like to know if he has had some early cases, such as some the otologists have operated upon. The otologists do make a diagnosis of the acoustic nerve tumors very early and some of them have taken the translabyrinthine route. For these large tumors that would be impossible, but for the early cases the translabyrinthine route has been practised successfully quite a number of times. Five or six surgeon otologists have been most successful so far as the life of the patient was concerned. One of the German surgeons who had had a tremendous mortality

from the approach Dr. Cushing describes, in the only case in which he made a translabyrinthine operation, had a success. All the others, although otologists, succeeded in removing tumors of the acoustic nerve without a single death. They were all small tumors and the diagnosis was made early. The superior petrosal sinus was wounded twice, but the bleeding was easily controlled by pressure. I wonder if Dr. Cushing has had any cases he could approach, or would favor approaching, by this particular route?

DR. G. J. HEUER: As Dr. Cushing has indicated, the attempt to enucleate tumors in the cerebello-pontine angle has been attended by a high mortality; and he has therefore been led to adopt a palliative rather than a radical procedure in the treatment of these lesions. By bisection of the tumor with removal of tumor tissue from within its capsule; in other words, by leaving that portion of the tumor in contact with the pons undisturbed, he has avoided injury to the pons and lessened the danger of respiratory paralysis. It is not an ideal procedure, for recurrence of the tumor is certain. Yet until earlier diagnosis and earlier operation make radical extirpation possible without too great danger to the patient, we should perhaps be content with it.

DR. BARKER: With regard to early diagnosis, ordinarily one has to deal with pressure symptoms, deafness associated with tinnitus, or with dizziness or staggering. It seems to me desirable that practitioners should have the aid not only of trained neurologists, but also of a skilled otologist for special analysis of the cochlear and vestibular functions and particularly for the several Bárány tests.

What Dr. Cushing has said about the nature of these growths interests me very much. I think we ought to keep in mind the exact position of what we call the cochlear and vestibular nerves. These nerves do not correspond to peripheral spinal nerves in the ordinary sense at all, but rather to their posterior roots, since corresponding to the posterior root ganglia of the spinal nerves are the ganglion spirale and the ganglion vestibulare of the labyrinth. When we recall the histogenesis of the posterior root ganglia and remember that the ganglia of the cerebral nerves have a similar origin, you will understand that there can easily be in the posterior root ganglia, and also in the nerves between them and the central organ, structures that correspond to the framework of the central system. In this framework there are two main types of cells, the spongioblast type and the pure neuroglial type. The pictures Dr. Cushing has shown are suggestive to my mind of the possible presence of both types of framework cells in these growths, not unlike those occurring in retinal gliomata. Dr. Councilman has also apparently seen true glial fibers in these tumors.

DR. CUSHING: As Dr. Halsted says, the translabyrinthine operation was originally proposed by Panse and five or six operations have subsequently been attempted. It seems to me that there are obvious drawbacks to this method of approaching the lesion, for it is evidently suitable only for very small tumors largely limited to a dilated porus internus. Moreover, the procedure leaves no decompression area which could offset the possibility of future growth of an incompletely removed tumor. It is inevitable, too, after such an operation that there should be a subsequent cerebrospinal fluid leak, and a good chance, therefore, of meningitis. The operative wound in cases of a brain tumor should unquestionably always be closed without drainage.

Then, too, the difficulty of making a diagnosis before you have something more than a disturbance of vestibular function with increasing deafness is very great. Few people would be willing at this early stage to submit to an operation of such magnitude as the translabyrinthine operation. It is too heroic a procedure for the existing symptoms at the time when it offers a possibility of success.

I do not believe that a surgeon is likely to expose an acoustic tumor, except as an accidental finding, of such a size that it can be

totally enucleated, though Dr. Heuer tells me that you have had such a case here. The true acoustic neurofibroma cannot be enucleated as can the pseudo tumors of the peripheral nerves, and in attempting a complete enucleation the facial must necessarily be sacrificed together with the remains of the acusticus.

The enucleable tumors, in my experience, are tumors which do not arise from the nerve but rather from the meninges, pressing the nerves of the recess, the acusticus included, off to one side. These tumors are fibro-endotheliomas and are easily shelled out, though their removal is not absolutely total, for one is bound to leave the stalk of attachment, which offers a possible source of a recurrence of the growth. I have had some 60 of these tumors, several of them arising from a point which might have made them simulate an acoustic tumor, and it is important that they should be clearly distinguished from one another.

I am sorry to say that as yet the Bárány tests do not help us materially in arriving at a diagnosis, though they are interesting, of physiological importance, and should be carried out in all cases, if for no other reason than to improve our knowledge of vestibular function.

In regard to the pathology of these lesions, we had little idea, until we had assembled the entire group of 30 tumors, how very similar they were. Just what they ought to be called is not clear, and it is for this reason that I have accepted the non-committal term of "acoustic tumor." Possibly neurofibroma would be the best designation, though many of the tumors in the series had been called endotheliomas by numerous pathologists in the past. Some of the peripheral tumors in cases of von Recklinghausen's disease have practically the same architecture and are evidently lesions which arise from the same or a very similar *Anlage*.

FEBRUARY 19, 1917.

1. Medical and Other Studies in the East Indies. DR. W. C. MACCALLUM.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB.

FEBRUARY 12, 1917.

1. Elizabeth Fry, Quaker Philanthropist: Her Work for Prisoners and Insane. DR. HENRY M. THOMAS.
To appear later in the BULLETIN.
2. Thomas Holley Chivers, Medical Poet, Contemporary of Poe. DR. THOMAS R. BOGGS.

THE LAENNEC SOCIETY.

FEBRUARY 26, 1917.

1. The Complement Fixation Test in Tuberculosis with Besredka's Antigen.¹ DR. J. BRONFENBRENNER.

Referring to the value of auscultation as an aid in the early diagnosis of tuberculosis, Laennec wrote in the preface to his great work, "I may say that no one who has made himself expert with this method will have occasion to say with Baglivi, 'Oh, how difficult it is to diagnose the disease of the lungs!'"

In spite of the great contribution rendered by Laennec himself, in spite even of the epochmaking discovery of Koch, the early diagnosis of tuberculosis is still a problem to be solved, even as it was one hundred years ago in the days of Laennec.

The difficulties confronting the students of tuberculosis are many; but the problem especially is difficult because of the extreme pleomorphism of the clinical manifestations of tuberculosis and because of the peculiar lack of uniformity in the course of this disease in different individuals affected, depending on their sus-

ceptibility or individual resistance, which are often subject to temporary fluctuations.

Although methods for the early diagnosis of tuberculosis are still wanting, the wide distribution of this disease is fairly well established. In fact, tuberculosis, not unlike syphilis, must be constantly kept in mind in making a diagnosis, whatever may be the clinical picture of the case.

Unfortunately, the manifestations of syphilis are no less pleomorphic than those of tuberculosis and in many instances they may amazingly simulate the clinical picture met with in tuberculosis. In cases where material for the bacteriological diagnosis of tuberculosis is not at hand, the Wassermann reaction is practically the only method for the differential diagnosis in such instances. However, as the Wassermann test itself is not absolutely specific, and as, on the other hand, it is not always present even in cases with definite signs of lues, this test does not offer an absolute means of differentiation between the two conditions.

In the quest for a reliable method for a diagnosis of tuberculosis, numerous investigators repeatedly attempted to apply the new methods used in the diagnosis of other infectious diseases, but their attempts were crowned only with partial success. Thus the use of agglutination, precipitation, meiostagmin and epiphanin reactions was found to be of little diagnostic value. The remarkable usefulness of the Wassermann reaction especially stimulated the efforts of numerous investigators along the lines of the application of the Bordet and Gengon reaction for the diagnosis of tuberculosis. The earlier efforts in this direction were not very encouraging. This could be due to several causes. It is possible that (owing to the walled-off nature of the lesions and the slow process of the disease in certain cases) there may be none or a very small amount of immune bodies present in the circulation. Moreover, the concentration of circulating antibodies is subject to constant and quite marked daily fluctuation in the same patient. Besides, the antibodies in tuberculosis may not be of the nature of amboceptors to any great extent. Again, tuberculous amboceptor, as suggested by Davidowitch, may be more thermolabile than most others, and since complement deviation is usually performed with inactivated serum, the amboceptor may be largely destroyed in heating.² Thus the amount remaining in the serum may not be large enough to be detected even by the delicate method of complement fixation.

In addition to the difficulties due to the apparent peculiarity of the immune processes in tuberculous individuals and resulting variations in concentration of specific amboceptors, the lack of proper antigens seems to have been largely responsible for the irregularity in the results obtained by different authors in their study of the complement fixation in tuberculosis. A study of the literature on this subject reveals the fact that, of all the different antigens used, suspensions of living or dead bacteria were found most reliable; but even with such antigens, the results obtained were not entirely satisfactory. In 1913, Besredka succeeded in cultivating tubercle bacilli on an entirely new medium. The fact that on this medium the organism showed some hitherto unknown properties induced him also to try the antigenic properties of his new cultures for the complement deviation test. Successful results obtained by Besredka and Manoukhing in their preliminary experiments have since been fully confirmed in several laboratories. It has been found that complement deviation with Besredka's tuberculin gives a very high percentage (90-95) of positive results in cases of clinical tuberculosis and at the same time the occurrence of the reaction, in cases in which tuberculosis could not be detected clinically, is limited to less than 10 per cent. The antigen of Besredka consists of autoclaved filtered cultures of tubercle

¹ From the Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pennsylvania.

² It is known that about 50 per cent of hæmolytic amboceptor is destroyed by inactivation.

bacilli grown on a new liquid medium, composed of alkaline broth to which are added egg-white and egg-yolk.³

As this medium cannot be made in large quantities on account of its rapid deterioration and has to be made fresh every time, the composition of the antigen made from it may vary in different batches. First of all, the chemical composition of individual eggs, and the consequent variations in the amount of alkali necessary for suitable clarification, vary to a marked degree. Besides directly affecting the chemical composition of the antigen, these fluctuations in the medium may also at times enhance or inhibit the growth of bacteria and thus still further influence the respective values of different batches of tuberculin for complement fixation.⁴

Another important source of variation was found in the apparent strain specificity displayed by different tuberculous sera. It is easy to demonstrate that certain tuberculous sera may fix the complement in the presence of certain selected samples of Besredka and other antigens. Thus, among fifty cases of diagnosed tuberculosis, in eighteen only did we find fixation with every one of the three samples of Besredka's tuberculin. In twenty-six cases we obtained fixation with two samples out of three, and in two cases the fixation was obtained with one sample of tuberculin only.⁵ That the selective fixation with different antigens is due to the strain specificity, and not to some technical error, is evidenced by the fact that in many instances, in which the sera were examined repeatedly, the results of such examinations invariably confirmed the selective tendency on the part of the sera.⁶

³ This medium is made in the following way: The white and yolk of an egg are each diluted with 10 volumes of water and filtered through a hard paper (Chardin). The yolk solution is carefully clarified by the gradual addition of sodium hydroxide. Both solutions are autoclaved and kept separately. Just before using one mixes 10 volumes of the sterile alkaline veal infusion (prepared without peptone, salt or glycerin) with two volumes of the sterile egg-white solution and one volume of the sterile clarified egg-yolk solution. This mixture is put into sterile tubes and is used without further sterilization. As this medium deteriorates on standing, it should be made fresh each time. Our experience fully confirmed the statement of Besredka about the rapid growth of certain strains of tubercle bacilli on this medium. It is true not all the strains seem to grow with equal facility, but certain strains like H46 and H48 from Dr. Baldwin, H12, H29 and H31 from Dr. Theobald Smith, R3 from Dr. Paul Lewis, and H389 from Dr. W. H. Park showed very definite growth within the first few days after planting.

⁴ This consideration should be given a great deal of attention, as some of the batches of antigen sent to us by Professor Besredka were more anticomplementary than others without being more antigenic. Hence it is necessary to vary the amounts of tuberculin used for the test with each batch of antigen.

⁵ Among 4000 sera examined in collaboration with J. Rockman and M. J. Schlesinger, with a view of establishing the nature of these variations in the respective fixing power of different samples of Besredka's antigen, the reaction was found positive with one or more samples of this tuberculin in 232 instances. Each of the 232 sera thus selected was reexamined with seven different preparations of tuberculin. We found that in 167 cases (72 per cent) out of 232, the fixation was obtained also with at least four antigens out of seven used. Out of the remaining 65 cases, in 23 at least two tuberculins fixed the complement and in 12 cases the crude tuberculin of the New York Board of Health was the only one confirming the results obtained with the tuberculin of Besredka. In 30 cases out of this total of 232 the fixation occurred only with the tuberculins of Besredka.

⁶ The existence of strain specificity in tuberculosis may be one of the contributing factors in causing much variation in the results obtained by different investigators in the complement deviation test for the diagnosis of tuberculosis.

The greatest and most important source of variation in the antigenic value of different batches of Besredka's tuberculin lies, however, in another direction. Already in the beginning of the study it appeared that a number of sera giving a positive Wassermann reaction often also showed fixation with Besredka's tuberculin. As one could not find clinical evidence of tuberculosis in all of these cases, the first explanation for this coincidence of the two reactions naturally was that the sera of syphilitics, having a high lipotropic coefficient, also fixed the complement with the tuberculin of Besredka on account of lipoids contained in it. The study of a number of sera giving a positive Wassermann reaction with this point in mind showed, however, that the complement deviation test with Besredka's antigen is not lipotropic in nature. Whenever present in sera possessing high lipotropic properties it depends on the presence of a separate antibody having its own index different from the lipotropic index in the same serum. Moreover, when the serum deviates the complement in the presence of both Besredka's tuberculin and pure lipin antigen, each of the two antibodies can be exhausted from such serum independently of each other. On the other hand, Besredka's tuberculin can be freed of its lipins without losing its property to fix complement in the presence of tuberculous sera. The lipins may be extracted by fat solvents, but the easiest method was found to be that of separation of the protein fraction by precipitation.⁷

The presence in the same serum of the property to fix complement with both antigens independently can be reproduced in experimental animals. When present in human beings (as well as in animals), the lipotropic antibody disappears under salvarsan treatment, whereas the tuberculous antibody persists.

The high percentage of negative reactions among clinically non-tuberculous (92 per cent), together with the other proofs of the high degree of specificity of this reaction, seem to indicate that the comparatively frequent simultaneous occurrence of the complement deviation test with Besredka's antigen and the Wassermann reaction in syphilitics is not due to some technical error.⁸

In fact the study of a number of cases from this point of view brings out some very interesting statistics. Thus Jones,⁹ subjecting to the Wassermann test 251 unselected cases coming to the public tuberculosis clinic, found that 73 among them had a positive Wassermann. In the series of 346 tuberculous inmates of the Boucicaut Hospital 19 per cent gave a positive Wassermann test, according to Letulle,¹⁰ and of these only 10 individuals (out of 64 reacting) were aware of their syphilitic infection or had definite signs of it. Our own results as well as these and other similar observations of different authors, which have come to our attention since our earlier work was published, suggest that occurrence of the complement fixation with Besredka's antigen in the cases in which the Wassermann reaction is also present may be due to the fact that either syphilis as such, or the antisyphilitic treatment, markedly lowers the resistance of the patients so as to make them either more susceptible to new infection with tuberculosis or to render them less resistant against the progress of this disease previously contracted.

Some of the authors, it is true, did not find any high frequency of occurrence of tuberculosis among syphilitics (as interpreted by

⁷ Such precipitation of the antigenic fraction of tuberculin also offers the possibility of using a standard number of units of antigen and thus eliminating variations due to the quantitative differences in specific properties of different samples of tuberculin, without increasing the chance of obtaining lipotropic reactions.

⁸ In this connection see results of Fraser, who, using various antigens both containing lipoids came to the conclusion that sera of syphilitics often deviate complement in presence of tuberculous antigens (bacillary emulsions). *Zeitschr. f. Immunitätsforsch., Orig.*, 1913, v, 20, p. 291.

⁹ Jones: *Med. Record*, 1916, Sept. 2.

¹⁰ Letulle: *Bull. de l'Acad. de Méd., Paris*, LXXVIII, No. 16, p. 589.

the complement fixation test). However, if one takes into consideration the class of patients upon which the test is performed, this discrepancy can be easily explained. In our series of syphilitics we dealt with patients of all ages, greatly exposed to infection with tuberculosis in their factory surroundings, and even more so in the unhealthy conditions of their lives in the slums. The material of Dr. Craig, who found less than 1 per cent of tuberculosis inluetics, for instance, consisted, on the contrary, of a group of young men of military age comparatively free from tuberculosis at the time of their admission to military service and who ever since their admission had been placed in exceptionally good hygienic conditions.¹¹ It seems, therefore, that for a non-selected group of patients (as represented, for instance, by the admissions to the general hospital or dispensary) the simultaneous occurrence of fixation with tuberculin and lipin is quite frequent and is due to the simultaneous coexistence of two diseases. Such a conclusion is apparently borne out by clinical observations of such men as Fournier, C. F. Marshall, Douty, F. H. Andrews, Sir Jonathan Hutchinson and others (see Oxford System of Syphilis, 1914, III, 197).

As for the percentage of the occurrence of the reaction in different stages of tuberculosis when a purified antigen of Besredka is used, we wish to present these approximate figures. First stage, 84 per cent; second stage, 94 per cent; third stage, 15.3 per cent; clinically non-tuberculous (controls), non-syphilitics, 5 per cent.

The question of the surprisingly low percentage of positive results in far advanced cases was especially investigated. In addition to the antigen of Besredka we examined a large group of such cases from Leech Farm, Pittsburg, with the antigens of Craig, Corper and Calmette and more recently also with the antigen of Miller. Although it was possible to observe a slight variation in the results obtained with the respective antigens, in general they reacted no better than that of Besredka.

As for the reason for this failure of advanced cases to give fixation there can be at least two offered tentatively; one is, that the resistance of the patient has been exhausted, there is no new antibody formation; and the other, that the circulating antibody is taken up as formed by the combination with antigen which may greatly increase during the last stages of the disease.

Although the results of experiments on animals in the case of tuberculosis can have only a relative value, the general tendency of the results also suggests that the concentration of circulating antibody depends on the degree of resistance of the animal. Thus, rabbits seem to develop antibody and show the fixation of complement if infected with the human strains of tubercle bacillus, but usually fail to fix complement when infected with bovine. In guinea-pigs the results are even more convincing. The animals give complement fixation already as early as the fourth or fifth day after infection, but uniformly fail to fix complement during the fourth to the sixth week of the disease.

Before closing I would like to give in brief the procedure followed in performing the test.¹²

Fresh serum is used, thus obviating the danger of destruction of antibodies due to heating. The human serum is titrated for the amount of complement present. Such titration is performed with

washed human red blood cells which have been previously sensitized with one unit of amboceptor. (The antihuman hemolytic system is used to avoid the uncontrollable factor due to the presence in human serum of varying amounts of natural antishoop amboceptor.) At the same time guinea-pig serum is titrated for its complement content, using human erythrocytes sensitized with the same amount of amboceptor. In setting up the test one adds a sufficient amount of guinea-pig serum to bring up the amount of complement already present in the human serum to two units. The antigen is then added and the tubes are incubated. At the end of the incubation, erythrocytes sensitized with one unit of amboceptor are added and after another period of incubation the progress of hemolysis is noted. We found this method to be very sensitive, its delicacy being entirely due to the minute amount of complement available for fixation and the absolute control of hemolytic system. Another advantage is in the fact that by using active serum we do not miss weak cases, where heating would have destroyed the antibody. As for the antigen to be used in the test, although we found Besredka's antigen to give the best results, we must admit, that the preparation of antigen as suggested by Miller and Zinsser is much simpler and, if the results obtained with it are as good as those obtained with Besredka's tuberculin, it seems that such antigen might be more practical for use in the test.

It is evident that a successful application of the complement fixation reaction for the diagnosis of early tuberculosis is already at hand.

There is very little doubt but that fixation indicates active tuberculosis, especially, if the reaction remains positive when repeated at intervals. In arrested or cured cases the reaction eventually becomes negative. The value of the negative outcome of the test is only relative (as it is also in the case of the Wassermann reaction), inasmuch as in advanced cases it is negative as well. In such cases the absence of circulating antibody may indicate the failing of resistance.

2. Complement Fixation in Tuberculosis. (Abstract.) DR. H. R. MILLER.

The phenomenon of complement fixation probably depends upon the fact that when an inciting organism invades the living body a reaction takes place between the serum of the host and the organism itself. In nearly all bacterial diseases this invasion is marked by a struggle the clinical manifestations of which constitute the picture of disease, and by a production of immune bodies or so-called antibodies. These antibodies (and here the term is used to represent diagnostic bodies rather than agents of any protective character) can be detected or measured in the blood of the host. In tuberculosis the most hopeful studies have been in the field of complement fixation of these antibodies. Enough work has already been done by the earliest investigators to demonstrate the value of the complement fixation in tuberculosis as a measure for diagnosis and prognosis.

In the main the technique of the reaction generally employed varied but little from the original Wassermann test; the antigens used varied greatly, however. These fall into four chief groups: (1) antigens prepared from the whole tubercle bacillus or any of its allied acid-fast bacilli; (2) tuberculins used as antigens; (3) tubercle bacilli extracts or derivatives, and (4) tuberculous or normal tissues employed as antigens.

Very encouraging results have been published with antigens of the types of Group 1 and Group 2, notably by the English workers who tried bacillary emulsions and by Besredka and his followers who worked with Besredka's tuberculin or modifications of it. Antigens of Group 3 and 4 have not been, comparatively, as useful as those of Group 1 and 2.

In February, 1916, Miller and Zinsser published results with a simple antigen made by grinding live tubercle bacilli with

¹¹ As a characteristic example of another extreme, proving the importance of ascertaining the social status of the patients on whom such tests are performed with the view of drawing conclusions as to frequency and interdependence of these two diseases, I wish to quote from Dr. N. B. Potter's article the results of Dr. Tedeschi, who found in his 10 years' service as a physician in a prison that 70 per cent of the cases of pulmonary tuberculosis had developed upon a luetic soil. (Tedeschi: Studium, Napoli, 1910, III, 343-377.)

¹² A detailed discussion of the technique will be given in the April issue of the American Journal of Syphilis.

ordinary table salt, and then adding distilled water up to isotonicity. This preparation may be used as it is or killed. It has given, and still gives, good results. There seems to be practically no false fixation of luetic or normal sera. With this antigen the test is positive in the largest proportion of Stage I, Stage II, and Stage III patients, yet in a number of cases of undoubtedly active tuberculosis the reaction is negative. For all practical purposes, however, the test is not positive in non-tuberculous persons, and is nearly always negative in arrested or quiescent tuberculosis and in luetic patients as well. The reaction is, therefore, an indicator of the activity of disease and does not point to the mere presence of tuberculosis. It does not parallel the tuberculin tests.

It seems fair to infer that a positive fixation implies absorption from active disease. In general, a negative reaction, except in those comparatively few instances where active disease is already present, signifies the absence of an active tuberculous process in the body.

DISCUSSION.

DR. PETROFF: The papers presented by Doctors Bronfenbrenner and Miller to-night were very interesting to me and important. Most of you know that this test has been revived in the last few years. The results obtained by different investigators in this country and abroad have justified drawing the conclusion that there is some value in the complement fixation test as performed to-day and that the clinician may be benefited by the test.

In the last few years several very good antigens have been introduced. Personally, I do not care what kind the other man is using. I am willing to discard my antigen for that which anyone else is using if it will give better results.

In my routine studies I have used three different antigens: (1) potato filtrate, which is similar to the bouillon filtrate of Denys and which is prepared from the filtrate of potato broth cultures; (2) sodium hydroxide extract of pulverized tubercle bacilli, and (3) methyl alcohol extract of dry pulverized tubercle bacilli. The potato filtrate and sodium hydroxide are my reliable antigens. The methyl alcohol antigen is at present only of experimental interest. After an extensive study of some 20 antigens, I came to the conclusion that there is no antigen which would act as a "shot-gun" preparation. If cases are not alive from a clinical standpoint, I do not see why they should be from a serological standpoint. I do believe in multiplicity of antibodies, and if there is multiplicity of antibodies there must be multiplicity of antigens. That is the reason why I use more than one antigen. We may obtain a positive reaction with the potato filtrate and not with the sodium hydroxide extract antigen, and vice versa. A positive reaction with either very likely means active tuberculosis.

Every patient admitted to the Trudeau Sanatorium is given the following tests and examinations: complement fixation, tuberculin skin test, X-ray and physical examinations. Every Monday we get together and the cases in question are discussed. If there is any discrepancy, such a patient is put on exercise which very often decides the question of active disease.

We have divided our cases into three main groups: clinically active, apparently cured and quiescent, and several minor groups. If we take the first two groups of cases which are classified from the clinical standpoint, namely the clinically active and the apparently cured, we find that the complement fixation test is positive in over 90 per cent of the active cases, and negative in approximately the same percentage of the apparently cured. This probably means that a positive reaction indicates an active disease.

However, there is a group of cases which puzzles the clinicians, and very often it will be found that not two of them agree about activity in such cases. Cases in this group are quiescent and are on the borderline dividing the active from the apparently cured. A case belonging to this group may give us a positive complement fixation to-day and a negative reaction a few days later, or vice

versa. Mild or violent exercise may cause the appearance of the positive reaction in a case where the reaction has been negative. A positive or negative reaction does not mean anything when the test is done only once. The blood of such quiescent cases must be studied every month, and only then may the findings bear some weight.

The complement fixation and the tuberculin skin test do not correlate in the early stage of the disease. But as the disease progresses toward a fatal termination, they correlate.

There are some conditions which may bring about a positive complement fixation where on previous examinations the test has been negative. An apparently arrested case with a negative fixation will during a cold give a positive reaction. The same results may be found after a general tuberculin reaction.

Now, a few more words before I close. The test is simple and may be run parallel with the Wassermann test. Much more work must be done before we can say that it can be adopted as a standard test. The test is not infallible, and a diagnosis based only on this test, disregarding the X-ray and physical findings, is deceptive. We are not yet sure of our interpretation of the test. I believe that complement fixation as applied to tuberculosis is much more specific than the Wassermann test. It is a true antibody antigen reaction. But I must confess that we have not yet the ideal antigen. The complement fixation has been established as an important test, and its future depends on the standardization of the antigen.

DR. KRAUSE: It has always been the hope of Dr. Baldwin, who for 25 years has stood in the forefront of tuberculosis investigation in this country, that some one would give us some method, some short cut, which would show us the difference between what we call clinical tuberculosis and those tuberculous changes that need no treatment, which may go on without manifesting themselves or being brought to the attention of the patient. Anything that would do this would mark the greatest advance and as an event in the history of tuberculosis would be comparable to the discovery of the bacillus itself.

The great majority of people who become diseased with tuberculosis do not need a strictly laboratory diagnostic method to detect that they have tuberculosis. But there continues to be a large number of cases which are on the borderline; a number of cases for which we have practically no method of determining whether they need treatment or not. We may have our opinion about this, but when we see the results of hasty diagnosis of tuberculosis, when we see what the stigma may mean and how tuberculous people react upon their environment, we begin to have some respect for a diagnosis of tuberculosis. In those cases that may be called concealed, the more or less quiescent cases, complement fixation would be of tremendous value if it would diagnose them and if we were certain of what the reaction meant. In advanced cases we would not need it so much, unless we were sure that it had some prognostic value. In the manifestly active cases we would not need it. But it is just these quiescent cases that are the ones for which we must perhaps have some kind of test if we are to make any advance over whatever methods we now have. I confess that it has always seemed inconceivable to me that there could be any biological test that would serve as an index of shadings and changes of activity or inactivity that are so fine and delicate as those we meet with in tuberculosis. Infection a test may show, and we would expect that some tests might reveal the presence or absence of frank activity of disease, although I would have you remember that the most practical fixation test, the Wassermann test, tells us little more in practice than that a man is infected. It will not differentiate symptomatic or active syphilis from latent syphilis.

I believe that all the work now going on in complement fixation in tuberculosis shows this, that there are a great many different types of antigen which will tell us that tuberculosis is at

work in the body, probably causing symptoms. I do not think though that the time has arrived when anyone should diagnose a case of tuberculosis on a complement fixation test alone. Every clinic that can should work hard at this test and gather observations made on the blood of patients who are suffering from all kinds of maladies. In the last analysis the place to work out this test is on experimental animals. It is here that we need most work.

DR. BRONFENBRENNER: Unfortunately, I am not situated as Dr. Petroff. I have no clinical material within reach and very often I am unable to examine the case twice, unless going back to the same test tube. However, I am aware of the fact, noted by others, that there are daily fluctuations in the antibody concentration in the serum of tuberculous individuals. My results have been obtained mostly on material sent to me sometimes from New York, sometimes from Chicago and only occasionally have I had it on the premises. The results stated by me have been published and I wish to refer Dr. Petroff to these publications where he will find more detail.

I had also among my cases a few where the tuberculosis was quiescent, and the reaction was strong. Among the cases with positive reaction there were also a few cases in which no clinical tuberculosis was disclosed by the physician in charge. However, at least two such cases went to Saranac Lake, and the diagnosis of tuberculosis was confirmed there clinically.

As for the experience of Dr. Petroff with complement fixation in rabbits, which all fixed the complement, even the controls, I think he makes a mistake somewhere. True, the rabbit is not a very reliable animal for the study of experimental tuberculosis, nor for complement fixation work, but in performing a number of experiments one still can draw conclusion as to the general tendency of the results. In my experience, though the majority of rabbits infected with human tuberculosis gave fixation, those infected with bovine bacillus as well as control (normal) rabbits practically never gave fixation with lipoid-free antigen.

The question of the co-existence of syphilis and tuberculosis is very important. I wish to repeat that in the great majority of cases, where I found both reactions present, there was clinical support for such serological findings supplied sometimes before and at other times after the serological examination had suggested the need of more complete clinical examination of the patient.

As for the sensitized cells, they are prepared by preliminary incubation of a suitable amount of amboceptor with washed red cells in proper concentration. It is very important properly to titrate the amboceptor for such a sensitization, for the excess of amboceptor causes hypersensitization of cells and that in turn entirely changes the quantitative relations of reagents in hemolysis. The proper amount of amboceptor for sensitization is determined as follows:

Place in several test tubes varying amounts of amboceptor solution and bring up the volume of 0.8 c. c. with physiological salt solution, then add 0.2 c. c. of the 50 per cent suspension of washed human red blood cells. Incubate for one-half hour in the water bath at 37° C. shaking occasionally. This results in 1.0 c. c. of a 10 per cent suspension of red blood cells sensitized with varying amounts of amboceptor. At the end of the half hour allowed for sensitization, distribute 0.025 c. c. of fresh human serum (human complement) into as many test tubes as there are dilutions of amboceptor above, and bring up the volume in each of these tubes to 0.9 c. c. These tubes then each receive red blood cells sensitized with gradually decreasing amounts of amboceptor. (This is done by transferring to each of them 0.1 c. c. from the various tubes above.) We have then a series of tubes each containing 1.0 c. c. of 1 per cent suspension of blood cells sensitized in the presence of varying amounts of amboceptor, and 0.025 c. c. of human serum. Incubate them at 37° C. for one-half hour and read the amount of

hemolysis in the tubes. The smallest amount of amboceptor which has sensitized 0.1 c. c. of 10 per cent red blood cells so that they are completely hemolyzed by 0.025 c. c. of fresh human serum constitutes one unit of amboceptor.

DR. MILLER: Although the subject in some ways seems more confused to-night than I had thought likely I believe there are certain things fundamental upon which we can all agree. This is a biological and not a mathematical test, and we must bear in mind that if it is helpful at all in detecting any number of cases, no matter how small, where the clinician has had trouble in diagnosis, it is worth while. We must also agree upon a uniform way of reading our tests. We must decide whether 4 plus means something or nothing. We must disregard a great deal of theoretical consideration and try to see if there is any practical value in this reaction. We should prepare as many antigens as possible and get at the data of their relative usefulness.

I think it is important not to use active serum. Very few, if any, antibodies are destroyed in the heating. In the Board of Health of New York City, for instance, it is a routine procedure to keep the already inactivated serums 12 to 14 days for retesting, if necessary. By simply reactivating the serum the test holds just as well. It is well known to many serologists that serum will sometimes contain a great deal of natural antisheep amboceptor which may be absorbed by the addition of red blood cells. To avoid error it is desirable to inactivate the supernatant fluid; the test will not be interfered with. I think, too, that in the use of active serum there lies the danger that with the employment of some kinds of antigens, a false fixation is possible. Inactive serum is preferred by most workers.

There does not seem to be a great deal of strain specificity. If the tubercle bacillus strain is good for antigen, one can definitely depend upon the strain and it will behave constantly and properly. For that reason, a single strain alone may give very satisfactory results. Polyvalent strains should be used, nevertheless. I think it is instructive to note that when one gets a positive result, in spite of clinical data and experiences, the same result is obtained with all antigens.

As for a relationship between positive Wassermann reactions and fixation with tuberculous antigen, in our laboratory we have not found cross fixation. The New York Board of Health sent us about 200 positive Wassermann sera, and we found them all negative but four; of these four two showed tuberculosis and in two the diagnosis was not excluded. We do not get cross fixation, nor do we, as a rule, get a positive reaction in normal patients, or in patients who have no tuberculosis. We do very occasionally get a positive fixation which we cannot explain.

It must be remembered that serologists have pointed out that the Wassermann reaction also fluctuates from time to time for the same patient, and also that we know very little about the underlying causes of the Wassermann reaction, for it is possible to obtain fixation of luetic sera with a great many different antigens: streptococci, colon bacilli, spirochætæ, various fat preparations, etc. It is my purpose to emphasize the need for continuing the work of cross fixation in tuberculosis and to point out that, after all, although it may at times appear to be not conclusive, it may, on the other hand, offer certain help. In a small percentage of positive cases the test is negative, but, after all, this may not invalidate the value of the reaction.

I would like to say a good word for the antigen we prepare and emphasize that it is worth using, because it is very simple to make; it requires no great preliminary preparations, its anti-complementary dose is far above the antigen dose, it keeps well and with it the results have not been inferior to those obtained with other preparations.

In conclusion, I think all the evidence points to the fact that the complement fixation reaction is a test that has come to stay.

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Physiology
N. H. L.

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HÆMOLYTIC SUBSTANCES IN HEATED MILK AND IN MILK CULTURES OF BACTERIUM WELCHII.

By WILLIAM W. FORD and JOSEPH H. LAWRENCE.
(From the Bacteriological Laboratory, The Johns Hopkins University.)

Milk heated to temperatures above 60° C., in which the non-spore-bearing bacteria are destroyed, decomposes from the multiplication of the aërobic and anaërobic spore-bearing bacteria which are always present. In a large proportion of the samples of milk obtained from the Baltimore markets an explosive reaction occurs which is usually due to the multiplication of *Bacterium welchii*¹ (*B. aerogenes capsulatus*). Sterile milk inoculated with this organism in pure culture shows a similar explosive reaction but the liquefaction observed in the samples of heated market milk is lacking. *Bacterium welchii* does not peptonise casein and the liquefaction found in the market milk must be due to other bacteria, probably to the aërobic spore-bearers.

The whey from the decomposed market milk sometimes has poisonous properties. If it be injected intravenously into rabbits these animals occasionally die with some of the symptoms of protein intoxication. Neutralization of the whey, which is often highly acid, at times does away completely with the toxic property of the milk but not in all instances.

The subcutaneous injection of the whey may also be toxic to rabbits which show an œdema at the site of inoculation, a fluid tinged with hæmoglobin in the peritoneal cavity and a hæmoglobin-stained urine. Neutralized whey is sometimes without this action upon animals. In other cases, however, the animals succumb in a few days and at autopsy show a subcutaneous œdema, a clear red fluid in the peritoneal cavity and a urine tinged with hæmoglobin. These findings all point to a hæmolytic intoxication and suggest that the decomposed milk may owe its poisonous properties in part at least to hæmolytic substances in addition to the excessive acidity. The poisonous action of heated and decomposed milk as well as the poisonous action of milk inoculated with pure cultures of *Bacterium welchii* is now being made the subject of further study. In order to elucidate it, however, it was first necessary to investigate the hæmolytic action of the whey from decomposed milk and from pure milk cultures of this organism. The results of this work seemed of sufficient interest to report at the present time.

HEMOLYTIC SUBSTANCES IN DECOMPOSED MARKET MILK.

Samples of Baltimore market milk heated to 85° C. for 15-20 minutes and incubated at 22° C. or at 37° C. for 24-48 hours explode violently with or without a subsequent peptonization. The fluid from such decomposed milk after filtration has hæmolytic properties for a variety of blood corpuscles. The bloods of rabbits, guinea-pigs, chickens and pigs are all sensitive and in about the same degree. The following table shows the hæmolytic activity of a typical sample:

TABLE I.

HEMOLYTIC ACTION OF FLUID FROM DECOMPOSED MILK.

Sample quantity.		Rabbit's blood, 5 % suspension.		Hæmolysis.
1.00 c. c.	+	1 c. c.	=	Complete.
0.75 c. c.	+	1 c. c.	=	"
0.50 c. c.	+	1 c. c.	=	"
0.25 c. c.	+	1 c. c.	=	"
0.10 c. c.	+	1 c. c.	=	Partial.
0.05 c. c.	+	1 c. c.	=	Negative.

All tubes made up to a total bulk of 3 c. c.
Control 1 c. c. NaCl 0.75% negative.

In this sample complete hæmolysis of 1 c. c. of 5 per cent rabbit's blood was produced by 0.25 c. c. of the filtered whey. Other samples of milk treated in the same way were also hæmolytic. The strength of the hæmolysin varied somewhat with the character of the milk and somewhat from day to day. It usually began to appear within the first 24-48 hours, increased slowly and reached its maximal intensity on the sixth or seventh day, after which it remained stationary for a time and then slowly deteriorated. The most active hæmolysins found were those in which complete solution of 1 c. c. of 5 per cent rabbit's blood was produced by 0.05 c. c. quantities equaling a dilution of 1-20. These were exceptional, however, the usual strength being 0.1 to 0.25 c. c. The hæmolysins proved fairly constant in the samples of milk treated in this way. The following table illustrates the strength of the hæmolysins found in a series of samples examined on one day:

TABLE II.

HEMOLYSINS IN SAMPLES OF DECOMPOSED MARKET MILK.

Sample.	Quantity necessary to give complete hæmolysis of 1 c. c. 5 % rabbit's blood.	
C.	0.75	
N.	0.5	
N.	0.75	
S.	0.5	
H.	0.1	
W.	0.25	

All the specimens gave cultures of *Bacterium welchii* on rabbit inoculation.

The hæmolysins in these milks were not typical, however, since with the lower dilutions the blood took on a dark-brown color like that due to methæmoglobin. In the higher dilutions the reaction was more characteristic, the tubes showing clear solutions tinged red with hæmoglobin. On testing with litmus the whey was found to be acid in reaction. If this acidity was carefully neutralized by sodium bicarbonate and the neutralized whey then tested, beautiful clear hæmolysins were found like those produced by other hæmolytic agents. This is shown in the following table which gives the reactions of

two characteristic samples. The hæmolytic action of the acid material is slightly greater than that of the neutralized.

TABLE III.

ACTION OF WHEY ON RABBIT'S CORPUSCLES BEFORE AND AFTER NEUTRALIZATION.

Sample.	Quantity used with 1 c. c. 5 % rabbit's blood.				
	0.1 c.c.	0.075 c.c.	0.05 c.c.	0.025 c.c.	0.01 c.c.
H. before neutralization	+	+	+	+	Trace
H. after neutralization	+	+	+	+	0
W. before neutralization	+	+	+	+	Trace
W. after neutralization	+	+	+	+	0

Control NaCl negative.
+ + = Complete hæmolysis.
+ = Partial hæmolysis.
0 = No hæmolysis.

The hæmolytic substances in this decomposed milk, therefore, are not the result of the acids (butyric and lactic) found in such milk, since they are present after neutralization. They react like true bacterial hæmolysins. This was borne out by a study of the thermal death-point, which lies between 55° C. and 60° C., as can be seen from the following table:

TABLE IV.

THERMAL DEATH-POINT OF HEMOLYSINS IN WHEY OF DECOMPOSED MILK.

Sample.	Quantity used with 1 c. c. of 5 % rabbit's blood.			
	1.0 c. c.	0.5 c. c.	0.25 c. c.	0.1 c. c.
Neutralized raw	+	+	+	+
Heated to 55° C. ½ hour....	+	+	+	+
Heated to 60° C. ½ hour....	0	0	0	0

Control NaCl negative.
+ + = Complete hæmolysis.
+ = Partial hæmolysis.
0 = No hæmolysis.

The hæmolysin is thus thermolabile, being weakened by exposure to 55° C. one-half hour and destroyed at temperatures between 55° C. and 60° C. This thermal death-point corresponds to the thermal death-points of bacterial hæmolysins in general, which lie between 55° C. and 60° C. In addition to being thermolabile bacterial hæmolysins are usually precipitable by reagents which throw down proteins such as ethyl alcohol and are sensitive to the digestive action of pepsin and pancreatin. The hæmolysin in milk can be precipitated by ethyl alcohol as is shown by the following protocol:

HÆMOLYSIN IN DECOMPOSED MILK PRECIPITABLE BY ETHYL ALCOHOL.

A small quantity of whey from sample of decomposed market milk H., which gave complete hæmolysis of 1 c. c. 5 per cent rabbit's blood in a dilution of 1-20, was treated with several times its volume of 95 per cent ethyl alcohol. A fine, flocculent precipitate was obtained. This was collected on filter paper, dried and taken up in 0.75 per cent NaCl. On testing with rabbit's blood it was found to be powerfully hæmolytic. The filtrate was without action on corpuscles.

The hæmolysin was also sensitive to the action of pepsin and pancreatin. When mixed with these substances in dried

powder form, placed at 37° C. for 24 hours and then tested upon blood corpuscles, it is without blood-laking properties. This is shown in the following table:

TABLE V.

ACTION OF PEPSIN AND PANCREATIN ON HÆMOLYSIN IN DECOMPOSED MILK.

Specimen.	Quantity used for hæmolysis of 1 c. c. of 5% rabbit's blood.		
	1 c. c.	0.5 c. c.	0.25 c. c.
H.	+ +	+ +	+ +
H. plus pepsin	0	0	0
H. plus pancreatin	0	0	0
Pepsin in 0.75% NaCl.	0	0	0
Pancreatin in 0.75% NaCl. 0	0	0	0
+ + = Complete hæmolysis.			
0 = No hæmolysis.			

Heated market milk allowed to decompose thus contains an hæmolysin which may be classed as a true bacterial hæmolysin because of its thermolability, its precipitability by alcohol, its sensitiveness to pepsin and pancreatin. As has been shown by previous investigations,² such milk is heavily infected by aërobie spore-bearing bacteria belonging to the groups of *Bacillus subtilis*, *Bacillus mesentericus*, *Bacillus cereus* and *Bacillus albolactus*. These organisms are devoid of hæmolytic activity as far as we know. As noted above, specimens of market milk in Baltimore, which when heated to 85° C. for 15-20 minutes decompose violently, always contain *Bacterium welchii*. This organism has well marked blood-laking properties, as is shown especially by the investigations of Herter,³ McCampbell,⁴ Simonds⁵ and others, and the hæmolysin in this decomposed milk may well be attributed to the development of this species. It has furthermore been shown that the lactic acid bacteria in raw milk inhibit the development of the gas bacillus. Raw milk allowed to clot does not decompose violently and the whey does not contain *Bacterium welchii* under ordinary circumstances. If the hæmolysin in the heated and decomposed milk is to be attributed to the gas bacillus it should not be present in raw soured milk. This point was tested by taking a series of six milks, and dividing them each into two lots. One lot was incubated at 37° C. for 48 hours and then kept at room temperature. The highly acid whey from each was neutralized by sodium bicarbonate and tested upon blood corpuscles at the end of three days and again at the end of 14 days. It was devoid of hæmolytic activity on all occasions. The other lot of six samples was heated to 85° C. for 15 minutes, incubated for 24 hours at 37° C. These samples exploded violently and all but one of them showed true hæmolysins after the acidity was neutralized. Hæmolysins thus develop in milk heated to 85° C. and incubated, while they fail to develop in the same milk when allowed to sour normally. Since such samples of explosive milk always contain actively growing *Bacterium welchii* this organism is further implicated as the source of the hæmolysin. The difference between raw and heated milk is brought out in the following table:

TABLE VI.

ACTION OF WHEY FROM RAW AND HEATED MILK UPON RABBIT'S CORPUSCLES.

Sample.	Quantity used with 1 c. c. rabbit's blood (5 % susp.).				
	1 c. c.	0.75 c. c.	0.5 c. c.	0.25 c. c.	0.1 c. c.
A. raw	0	0	0	0	0
A. heated	+	+	+	0	0
S. raw	0	0	0	0	0
S. heated	+	+	+	+	0
S. F. raw.....	0	0	0	0	0
S. F. heated	0	0	0	0	0
A. S. raw	0 •	0	0	0	0
A. S. heated	+	0	0	0	0
C. raw	0	0	0	0	0
C. heated	+	0	0	0	0
W. raw	0	0	0	0	0
W. heated	+	0	0	0	0

From this table it may be seen that five of the six samples of heated milk showed hæmolytic substances varying in strength from 1 c. c. to 0.25 c. c., but that all the samples of whey from the raw milk were devoid of hæmolysins. The hæmolysin found in decomposed market milk can thus be attributed to the development of *Bacterium welchii*, which is known to produce blood-laking substances, provided its reactions are the same as those of the hæmolysin produced by this species. The hæmolysin of the gas bacillus is not usually regarded as a true bacterial hæmolysin but is attributed to the various acids produced in culture media by the growth of this organism, particularly to the butyric and lactic acids. Herter was inclined to believe that the hæmolysin was due to the acids because of its resistance to heat, while McCampbell attributed it to butyric acid which he says is hæmolytic in about the same degree as the acid cultures of the organism. It became necessary, therefore, to make a further study of the hæmolytic substances produced by *Bacterium welchii*, particularly in milk cultures.

HÆMOLYSINS IN MILK CULTURES OF BACTERIUM WELCHII.

From one of the flasks of market milk which after heating to 85° C. had been incubated and had shown an explosive reaction, a pure culture of the gas bacillus was obtained by the inoculation of a rabbit by the usual procedure. This organism was a large Gram-positive encapsulated bacillus giving the cultural reactions of *Bacterium welchii*. Two large flasks of milk were inoculated with this strain and incubated for 24 hours. They both showed the characteristic explosive reaction. The whey from each was collected carefully by pipetting it off from the mass of gas-eaten curd, filtered several times through filter paper and finally through a Berkefeld candle. The resulting clear solutions were found to be hæmolytic for rabbit's corpuscles in a dilution of 1-40. In the greater concentrations the tubes took on a dirty-brown color like that of methæmoglobin, suggesting that the hæmolysis was due to acid. After careful neutralization the whey was still hæmolytic to about the same degree as the acid material. The tubes no longer showed the dirty-brown color but were a clear scarlet, characteristic of hæmolysis not due to acid.

The action of the whey from cultures of *Bacterium welchii* before and after neutralization is shown in the following table:

TABLE VII.

HÆMOLYTIC ACTION OF MILK CULTURES OF BACTERIUM WELCHII.

Sample.	Quantity used with 1 c. c. 5 % rabbit's blood.					
	.05 c.c.	.25 c.c.	.01 c.c.	.0075 c.c.	.005 c.c.	.0025 c.c.
A.	+	+	+	+	Trace	0
A. neutralized.	+	+	+	+	+	Trace
B.	+	+	+	+	Trace	0
B. neutralized.	+	+	+	+	Trace	0

+ + = Complete hæmolysis.
+ = Partial hæmolysis.
0 = No hæmolysis.

NOTE.—The greater concentrations of whey were completely hæmolytic but have not been included in the table.

The hæmolysin in milk cultures of *Bacterium welchii* is thus independent of the acidity of the cultures. In the two samples of the above table it had a strength somewhat greater than that of the hæmolysin found previously in decomposed market milk, being present in 0.025 quantities, a dilution of 1-40. This greater development of hæmolytic activity may be due to the fact that in these flasks the gas bacillus was in pure culture and its growth was not interfered with by other organisms. It appeared usually within the first 24 hours, and in the samples thus far examined seemed to reach its maximal intensity on about the third day. Its appearance in the whey after neutralization of the acids present suggests that it is a true bacterial hæmolysin. This is borne out by a study of the thermal death-point, which lies between 55° C. and 60° C., as is shown in the following table:

TABLE VIII.

THERMAL DEATH-POINT OF HÆMOLYSIN OF BACTERIUM WELCHII.

Sample.	Quantity used to hæmolyse 1 c. c. 5 % rabbit's blood.			
	1 c. c.	0.5 c. c.	0.25 c. c.	0.1 c. c.
B. neutralized	+	+	+	+
Heated to 55° C. ½ hour.....	+	+	+	+
Heated to 60° C. ½ hour.....	0	0	0	0

+ + = Complete hæmolysis.
+ = Partial hæmolysis.
0 = No hæmolysis.

The hæmolysin of *Bacterium welchii* corresponds to the true bacterial hæmolysins in other respects. Thus it may be precipitated by ethyl alcohol, as is shown by the following protocol:

HÆMOLYSIN OF BACTERIUM WELCHII PRECIPITABLE BY ETHYL ALCOHOL.

The whey from a milk culture of *Bacterium welchii* was filtered several times through filter paper, then through a Berkefeld candle, neutralized by sodium bicarbonate and when tested upon rabbit's blood was found to have hæmolytic activity in a dilution of 1-40. It was treated with several times its volume of 95 per cent ethyl alcohol. A fine, flocculent precipitate was obtained. This was collected on a filter paper, dried, taken up in 0.75 per cent NaCl and found to be power-

fully hæmolytic to rabbit's blood. The filtrate was without action on blood.

The hæmolysin of *Bacterium welchii* is also sensitive to pepsin and pancreatin. Mixed with these substances and placed at 37° C. for 24 hours, active solutions of the hæmolysins lose their blood-laking properties, as is evident from the following table:

TABLE IX.

ACTION OF PEPSIN AND PANCREATIN ON HÆMOLYSIN OF BACTERIUM WELCHII.

Specimen.	Quantity used for hæmolysis of 1 c. c. of 5 % rabbit's blood.		
	1 c. c.	0.5 c. c.	0.25 c. c.
welchii	+	+	+
welchii plus pepsin.....	0	0	0
welchii plus pancreatin	0	0	0
Pancreatin	0	0	0
Pepsin	0	0	0

+ + = Complete hæmolysis.
0 = No hæmolysis.

The hæmolysin in milk cultures of *Bacterium welchii* is thus independent of the acidity of the cultures, is thermolabile, can be precipitated by ethyl alcohol and is sensitive to the digestive action of pepsin and pancreatin. It has the same characteristics as the hæmolysin in decomposed market milk, and the hæmolysin in the latter substance may reasonably be attributed to the development of this species. The possibility that other bacteria which produce hæmolytic substances may also be present in this milk must, of course, always be considered. The close correlation between the presence of the hæmolysins in milk and the presence of *Bacterium welchii* and the similarity in reactions of the hæmolysin in the heated market milk and of the hæmolysin in milk cultures of *Bacterium welchii* are both quite striking, however, and lend strong support to the view that this organism is the chief source of the hæmolysins in question. The hæmolysin of *Bacterium welchii* according to these observations belongs to the group of bacterial hæmolysins and is not to be attributed to any acids like butyric or lactic acid, which this species may produce in milk cultures. Both butyric and lactic acids are hæmolytic. When made up in a 1 per cent solution of the official acids they dissolve blood corpuscles rapidly, as can be seen from the following table:

TABLE X.

HÆMOLYTIC ACTION OF LACTIC AND BUTYRIC ACIDS FOR RABBIT'S CORPUSCLES.

Lactic acid, 1 % sol.		Rabbit corpuscles, 5 % suspension.		Hæmolysis.
.01 c. c.	+	1 c. c.	=	+ +
.0075 c. c.	+	1 c. c.	=	+ +
.005 c. c.	+	1 c. c.	=	+ +
.0025 c. c.	+	1 c. c.	=	+ +
.001 c. c.	+	1 c. c.	=	+ +
.00075 c. c.	+	1 c. c.	=	+
.0005 c. c.	+	1 c. c.	=	0
.0001 c. c.	+	1 c. c.	=	0

Control NaCl negative.
+ + = Complete hæmolysis.
+ = Partial hæmolysis.
0 = No hæmolysis.

Butyric acid, 1 % sol.		Rabbit corpuscles, 5 % suspension.		Hæmolysis.
.01 c. c.	+	1 c. c.	=	++
.0075 c. c.	+	1 c. c.	=	++
.005 c. c.	+	1 c. c.	=	++
.0025 c. c.	+	1 c. c.	=	++
* .001 c. c.	+	1 c. c.	=	+
.00075 c. c.	+	1 c. c.	=	0
.0005 c. c.	+	1 c. c.	=	0
.0001 c. c.	+	1 c. c.	=	0
Control NaCl negative.				
++ = Complete hæmolysis.				
+ = Partial hæmolysis.				
0 = No hæmolysis.				

Lactic acid thus hæmolyzes in a dilution of 1-1000 of a 1 per cent solution and butyric acid in a dilution of 1-400. The hæmolysed blood takes on a dirty-brown color characteristic of acid hæmolysis and never shows the clear solutions tinged with hæmoglobin produced by the true bacterial hæmolysins. Moreover, the hæmolysins of both lactic and butyric acids are thermostabile. If dilutions of 1-200 (.005 c. c. of a 1 per cent solution) be taken and tested for their power to resist heat it is found that their hæmolytic activity is not injured by exposure to high temperatures, even that of the boiling point. This is shown in the following table:

TABLE XI.										
ACTION OF HEAT ON HÆMOLYTIC ACTIVITY OF LACTIC AND BUTYRIC ACID.										
Hæmolysis of 5 % rabbit's blood heated ¼ hour to										
	Raw	50°C.	55°C.	60°C.	65°C.	70°C.	80°C.	90°C.	100°C.	
Lactic Acid	++	++	++	++	++	++	++	++	++	++
1-200										
Butyric Acid	++	++	++	++	++	++	++	++	++	++
1-200										

The thermostabile hæmolysin in milk cultures of *Bacterium welchii*, therefore, cannot be attributed to either butyric or lactic acid. That these acids may play a rôle in the hæmolysis produced by the whey before neutralization is not denied, but we believe that this action on the blood corpuscles is an independent phenomenon. The hæmolysin in the neutralized

cultures of *Bacterium welchii*, according to our present observations, is a true bacterial hæmolysin. Finally it is to be noted that the hæmolysins in decomposed market milk which we attribute to the presence of *Bacterium welchii* are also independent of both lactic and butyric acids, since like the hæmolysin in milk cultures of *Bacterium welchii* they are found in the milk after neutralization and are thermolabile.

SUMMARY AND CONCLUSIONS.

Market milk heated to 85° C. for 15-20 minutes and allowed to decompose by incubation at 22° C. or 37° C. for 24-48 hours contains an hæmolysin of moderate strength. This hæmolysin is independent of the acids in the milk, occurring in neutralized specimens, is thermolabile, being destroyed at temperatures between 55° C. and 60° C., is precipitable by ethyl alcohol and can be digested by pepsin and pancreatin. It is to be classed with the bacterial hæmolysins and is in all probability to be attributed to the presence of *Bacterium welchii* in the market milk. Pure milk cultures of *Bacterium welchii* contain a similar hæmolysin which is, however, usually slightly more powerful. This also is independent of the acids in the milk, is thermolabile, being destroyed at temperatures between 55° C. and 60° C., is precipitable by ethyl alcohol and can be digested by pepsin and pancreatin. On the basis of the work thus far completed we believe that this hæmolysin is a true bacterial hæmolysin. It is especially to be differentiated from the hæmolysin of both lactic acid and butyric acid, which are thermostabile. The rôle which these acids play in the hæmolysis seen in cultures of *Bacterium welchii* is, we believe, secondary to that of the true bacterial hæmolysin secreted by the organism.

BIBLIOGRAPHY.

1. Ford and Pryor: The Johns Hopkins Hosp. Bull., Vol. XXV, No. 283, 1914, p. 270.
2. Lawrence and Ford: Jour. of Bact., Vol. I, No. 3, 1916, p. 277.
3. Herter: Jour. Biol. Chem., Vol. II, 1906, p. 1.
4. McCampbell: Jour. Infect. Dis., Vol. VI, 1909, p. 537.
5. Simonds: Monograph of the Rockefeller Institute, No. 5, Sept. 27, 1915.

VENOUS CONGESTION IN ITS RELATION TO NECROSES OF THE LIVER.

By HORST OERTEL.

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It has become generally recognized that severe venous congestion in the liver may in a certain type of cases be associated with lobular necroses and that these may become extensive enough to lead to a very general disorganization of the liver substance, occasionally with deep jaundice, and clinically to coma and death. A discussion has arisen as to the cause of these necroses: A number of cases under my observation from 1903 to 1910 led me to the conclusion, stated first in a report of a case in the Archives of Internal Medicine (1910, vi, 293) and later in a general consideration of this lesion in the

Berliner Klinische Wochenschrift (1912, Nr. 43), that these necroses were directly dependent upon the stasis and were not bacterial or toxic in origin.

Mallory, on the other hand, in an extensive study of this subject (Journal of Med. Research, 1911, xxiv, 455), regarded them essentially as bacterial and toxic in character.

This question was investigated experimentally by Bolton (Jour. Pathol. and Bact., 1914, xix, 258), who was able to produce exactly similar necroses by causing extreme congestion in the liver by partial and complete obliteration of the

vena cava in the monkey. Based on his results, Bolton decided that the cellular loss was directly due to passive congestion and not to bacterial infection.

The recent observations of Heinrichsdorff (Ziegler's *Beiträge*, 1914, lvii, 635), and especially of Lambert and Allison (Bull. Johns Hopkins Hospital, 1916, xxvii, 310), on human livers, also place the greater emphasis on the congestion itself and subordinate the importance of infections or of outside toxic factors. Similar views are expressed by MacCallum (Text-book of Pathology, 1916, p. 469). Although it seems, then, that the combined anatomical and experimental evidence favors the direct relation of cyanosis to the production of necroses, there is as yet no agreement or certainty as to the exact manner in which these necroses develop. MacCallum, Lambert and Allison look upon the necroses of the liver cells as the result of asphyxia, Hart as due to a lack of nutrient material owing to the formation of fibrin plugs in capillaries, Heinrichsdorff even regards them as due to an autointoxication caused by the higher CO_2 contents of the blood and the entrance of intestinal, harmful substances acting on depressed, poorly nourished, liver tissue.

My studies have led me to a different idea, which has been strengthened by recent observations. It is based directly on the anatomical evidence of the nature of these necroses, which, to me, appears highly significant in regard to the genesis of the lesion. For this reason I have in previous publications repeatedly emphasized that we are not dealing with ordinary necrotic changes, ushered in by marked parenchymatous degeneration, nuclear degeneration, protoplasmic coagulation and the formation of dead structureless masses, but with simple cell solution. The cells undergo oedematous swelling, the protoplasm becomes honey-combed and gradually dissolves; the nucleus persists until late, when it, too, disappears by simple karyolysis; the cell outlines remain and become even more distinct as the protoplasm dissolves; ultimately remains nothing of the cells, only a fine reticulum occupies the parts implicated. Fat occurs usually in large drops at the periphery of these necroses.¹ In other words these changes, from the start, are similar to oedematous imbibition and solution, and not at all in the nature of direct cell destruction that occurs from the effects of bacterial or toxic injury. This latter leads early, as is well known, to severe degenerative pictures in the protoplasm and nucleus of the cell, to obscurity of the cell outline and coagulation of dead protoplasmic masses. But these features are entirely absent in cyanotic necrosis.

Furthermore, it does not seem that interference with nutrition by asphyxia or lack of nutriment alone would explain these characteristic histological findings. I consider their relation to these cell changes, as will be explained later, an indirect one.

Now it might be doubted that even an extensive oedematous imbibition of the liver (admitting this to occur as the result

of certain severe cases of cyanosis) would lead to such necroses. I have, however, been fortunate enough to be able to observe lately the liver in a case of fatal trinitrotoluene poisoning in a healthy, strong, muscular young man. (The case has been reported elsewhere by Dr. Odland, of this laboratory, Royal Victoria Hospital, Montreal, Scientific Reports, 1916, Series B. 1.) It appears that trinitrotoluene is essentially a vascular poison. It leads to massive oedema and hæmorrhages, but does not seem to display marked toxic affinity for the liver cells themselves. This liver presented histologically pictures very similar to cyanotic necroses, both in manner of formation and in the end product, viz., massive, intercellular oedema, followed by oedematous swelling, cytolysis and karyolysis of liver cells individually well outlined until late, without parenchymatous degeneration and coagulation necrosis. The end result was here also a hazy reticulum. The only difference from the changes in chronic cyanosis was a remarkable absence of fat in the surrounding liver cells, which are frequently very fatty in cyanotic necrosis.

Finally, a very similar, although more diffuse, type of cell degeneration and necrosis in the liver was observed by me several years ago in experimental uranium nephritis (A contribution to the knowledge of experimental nephritis, *Lancet*, May 23, 1914). Uranium, much like trinitrotoluene, produces in the liver as in the kidney a very marked oedema followed soon by tremendous swelling (hydrops) and solution of liver cells in a manner described above. As with trinitrotoluene, fatty changes are absent after the administration of large doses, whereas, on the other hand, oedema and cytolytic necrosis of the liver cells are most marked. I noted at the time that these changes are different from those caused by cantharidin and mercury, which display a pronounced toxic affinity for liver parenchyma as shown by definite parenchymatous degeneration and coagulation necrosis.

Based, then, on the characteristic type of necrosis in venous cyanosis and its similarity to others in which oedematous imbibition of liver cells also occurs, it seems to me reasonable to maintain, that, under certain conditions of severe cyanosis, increased transudation with stagnation occurs in the liver, as we know it to occur elsewhere. This leads primarily to passive swelling (hydrops) of liver cells, secondarily to their solution, possibly through the formation of a cytolytic ferment, and thus to characteristic liver necroses.

The extent and rapidity with which these form seem to depend, to some extent at least, upon the amount and stagnation of the transudate or oedema. Thus, they are more pronounced in severe advanced congestion. They assume, therefore, occasionally dimensions of such an extensive and often rapid disorganization of the liver as to lead to rapidly deepening jaundice and, clinically, to coma and death.

Finally, as to the cause of the oedema. Here, it seems to me, a number of factors contribute: First, impaired oxidation (asphyxia) of the cells and consequent accumulation of waste products lead to high osmotic pressure and increased

¹ The detailed description of the cell changes by Heinrichsdorff fully agrees with my own.

H ionization in the tissues;² secondly, increased transudation and lessened resorption of fluid result from diminished tissue tension and nutritional disturbances in blood-vessels and lymphatics. To these contribute further increased venous and lessened aortic pressure. Thirdly, gradual collapse of the lobule makes lymph circulation increasingly difficult and ultimately entirely impossible. This, together with hæmorrhages into the lost parts, hastens the terminal destruction of the lobule.

Although it appears that the accompanying jaundice is also a result of lobular disorganization, the exact manner in which

² See J. Loeb. *Pflüger's Arch.*, 1898, 71, p. 457, on the relation of osmotic pressure to œdema.

this is produced must, like that of jaundice generally, be still determined by future research.

It may be asked why the liver is involved in these, often severe and general, cyanotic necroses in preference to other parenchymatous organs (the kidney for example). This may be due to its architectural arrangement and characteristic blood and lymph flow in which it differs from other organs; for the parenchyma cells, in forming pyramids around the central veins and columns, which stand in intimate contact on either side with blood and lymph capillaries, possibly even through intracellular canaliculi, are in closest connection with their circulation and not separated by any elastic stroma or basement membrane. To this must be added the, even normally, much retarded blood and lymph flow in the liver as compared with that in other glandular organs.

OBSERVATIONS ON THE DEGENERATION OF LEUCOCYTES IN THE URINE AS A DIAGNOSTIC AID IN TUBERCULOSIS OF THE URINARY TRACT IN WOMEN.*

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In 1906 Colombino published the results of a cytological study of the urine in cases of pyuria, with reference to the diagnosis of tuberculosis of the genito-urinary tract. He concluded that in cases showing degenerated leucocytes and some red blood cells, a definite diagnosis of tuberculosis can be made.

These degenerated leucocytes are described as having variable forms; polyhedral, elongated and indented. In some cells the protoplasm seems to have been eaten out and considerably reduced about the nucleus. In other cells there are multiple vacuoles in the protoplasm and small balls of protoplasm at the periphery of the cells which seem detached from them. In many of these irregular cells the envelope seems to have burst. Free nuclei are also found.

Colombino attributed this degeneration to a specific toxic action of the tuberculous urine. He was unable to find any relation between the concentration, reaction or content in chlorides, phosphates, sulphates, urates and uric acid and the cytological picture.

Moscou, in 1907, reported a series of cases and the results of his studies on the cause of this degeneration. He concluded that it is independent of the reaction, concentration or content in urea and chlorides and that cryoscopic determinations shed no further light on the question, nor does the time of examination after voiding have any relation to the phenomenon.

Moscou added normal leucocytes to tuberculous urine and degenerated leucocytes to normal urine, but did not observe

any change in the contour of the cells in either case. However, he found that if degenerated leucocytes are placed in isotonic salt solution, they become normal in form after from five to twenty minutes, and that this also occurs if a solution of picro-carmin is substituted for normal salt solution.

Goldberg states that he observed, in 1901, elongated and spindle-formed cells in tuberculous urine and that leucocytes in ameboid action also were seen.

Colombino found the cytological formula of tuberculous and non-tuberculous urines to be nearly always the same:

Polynuclear neutrophiles	90 - 95%
Mononuclears	10 - 5%

In one case of very long standing pyelitis with calculus, there were 67 per cent of mononuclears, and in another similar case 12 per cent of mononuclears.

His series of cases included 20 of genito-urinary tuberculosis, in all of which degenerated leucocytes and red blood cells were found, whereas in 13 cases of non-tuberculous pyuria, the leucocytes were well preserved, except in one case of renal calculus of long standing.

In Moscou's series of 50 cases, there were 22 of genito-urinary tuberculosis. In 18 of these degenerated leucocytes were present; in four there was no degeneration. He also observed leucocytic degeneration in two non-tuberculous urines.

Goldberg reported degeneration of leucocytes in 13 and no degeneration in four cases of urogenital tuberculosis; no degeneration in eight cases of kidney or bladder stone, and deformed cells in eight cases of gonorrhœa (acute and chronic) in four of which the majority of the leucocytes had become degenerated.

* Read before a meeting of The Johns Hopkins Hospital Medical Society, May 7, 1917.

TABLE I.—TUBERCULOUS CASES. OPERATED.

Gyn. No.	Age	Operation.		Pathological.		Urine Examination.										Culture.		
		Date.	Character.	No.	Diagnosis.	Date.	Voided.	Cath.	Time after collection.	R. B. C.	Ep.	Casts.	Bacilli.	W. B. C.	Reaction.			
21625	38	10/25/15	Nephrectomy, right.	21617	Tuberculosis of kidney.	10/25/15	+	Immediate.	0	0	0	Non-motile rods. No tuberculous smears.	No Large amount of pus. Well preserved cells.	Well Acid.	From both kidneys. No growth.		
Med. 34925	21	Nephrectomy.	Tuberculosis of kidney.	10/29/15	+	Immediate.	+	+	0	Acid-fast bacilli.	Large amount of pus. Some degenerated cells. Majority well preserved.	Acid.			
Miss F.	..	12/8/15	Nephrectomy, left.	Tuberculosis of kidney.	11/4/15	+	Immediate.	+	+	0	Tubercle bacilli.	About 30% show degeneration.	Acid.			
						11/23/15	+	Several hrs.	+	+	0	Tubercle bacilli.	Large amount of pus. Majority of cells degenerated.				
F. 47637	52	1/5/16	Nephrectomy and ureterectomy, left.	21798	Tuberculosis of kidney.	12/3/15	+	1 hour.	+	+	0	Tubercle bacilli.	Large amount of pus. Majority of cells degenerated.		B. coli, bladder and left kidney.		
21859	12/2/15	+	Immediate.	+	0	Tubercle bacilli. Non-motile rods.	Large amount of pus. Majority of cells degenerated.	Acid.			
21813	21	12/17/15	Nephrectomy, left.	21764	Tuberculosis of kidney.	12/9/15	+	Immediate.	+	+	0	Tubercle bacilli.	Same as above.		Staphylococcus albus bladder abscess. No growth.		
19972	22	2/19/14	Nephrectomy, right.	19960	Tuberculosis of kidney, right. Now tuberculosis of left kidney.	12/15/15	+	Immediate.	+	+	0	Tubercle bacilli.	Moderate amount of pus. 90% degenerated.	Neu- tral.			
						2/18/16	+	24 hours.	+	+	0	Tubercle bacilli.	Moderate amount of pus. 90% degenerated.				
						5/2/16	+	24 hours.	+	+	0	Tubercle bacilli.	As above.				
22040	24	3/22/16	Nephrectomy, left.	22002	Tuberculosis of kidney.	11/2/16	+	48 hours.	+++	+	0	Tubercle bacilli.	As above.		Bladder and kidneys, right and left. No growth.		
						3/8/16	+	Immediate.	+++	0	Tubercle bacilli.	Small amount of pus. Majority well preserved. About 20% degenerated.	Neu- tral.			
						3/18/16	+	8 hours.	+	+	0	Tubercle bacilli.	As above.	Neu- tral.			
						3/20/16	+	Immediate.	+++	0	Majority well preserved. 20% irregular in outline.						
22366	18	6/13/16	Nephrectomy, right.	22281	Tuberculosis of kidney and tuberculosis of bladder.	4/18/16	+	8 hours.	0	+	0	A few W. B. C. well preserved.	Acid.	No growth.		
						4/24/16	+	Immediate.	+	+	0	Tubercle bacilli.	A few W. B. C. well preserved.	Acid.			
						4/18/16	+	Immediate.	0	0	0	0	0	0		0	Acid.
						4/18/16	+	Immediate.	0	+	0	Tubercle bacilli.	A few W. B. C. well preserved.	Acid.			
22709	33	11/27/17	Nephrectomy and ureterectomy, right.	22681	Tuberculosis of kidney and ureter.	11/14/16	+	30 hours.	0	+	0	Tubercle bacilli.	Moderate amount pus. 40% degenerated.	Acid.	No growth.		
Brooks	40	Nephrectomy, right.	22803	Tuberculosis of kidney.	11/15/16	+	5 hours.	+	+	0	Tubercle bacilli.	Moderate amount pus. 75% degenerated.	Acid.			
						11/27/16	+	Immediate.	0	0	0	Tubercle bacilli.	Moderate amount pus. A few degenerated W. B. C.	Acid.			
						12/14/16	+	Immediate.	+	0	0	Short motile rods.	Large amount pus. Majority degenerated.	Acid.			
Miss M.	18	2/23/17	Nephrectomy, right.	22858	Tuberculosis of kidney.	12/28/16	+	Immediate.	0	+	0	Tubercle bacilli.	As above.		No growth.		
						2/21/17	+	Immediate.	+	+	0	Tubercle bacilli.	Large amount pus. About 5% degenerated.	Acid.			

TABLE II.—NON-TUBERCULOUS CASES. OPERATED.

Gyn. No.		Operation.		Pathological.		Urine Examination.										
		Date.	Character.	No.	Diagnosis.	Date.	Voided.	Cath.	Time after collection.	R. B. C.	Ep.	Casts.	Bacilli.	W. B. C.	Reaction.	Culture.
21599	80	11/6/15	Nephrotomy, right.	21662	Nephrolithiasis, right. Chronic interstitial nephritis.	11/6/15	+	1½ hours.	0	+	0	Chains of cocci.	Large amount pus. Well preserved cells. A few slightly irregular in outline. No marked degeneration. Not as well preserved as usual.	Acid.	Streptococcus.
22322	..	6/20/16	Nephrotomy, right.	22316	Nephrolithiasis, left.	6/20/16	Aspirated from kidney at operation.	Immediate.	+	0	0
21700	55	1916	Nephrolithotomy, left.	Bilateral nephrolithiasis.	11/23/15	+	Immediate.	++	+	0	Motile rods.	Large amount pus. Well preserved cells. Occasional slightly degenerated cells.	Acid.	B. paratyphosus.
					Died after operation.	11/23/15	+ right kidney.	Immediate.	+++	+	0	Motile rods.	Large amount pus. Well preserved cells. A few degenerated cells.	B. paratyphosus.
					Streptococcus cellulitis around wound.	11/23/15	+ left kidney.	Immediate.	+	+	0	Motile rods.	Moderate amount pus. Well preserved cells. Occasional slightly degenerated cells.	B. paratyphosus.
21716	38	12/2/15	Repair of post-operative vesico-vaginal fistula.	11/29/15	+	+	Several hrs.	0	+	0	0	A few W. B. C. Well preserved.	Acid.	
					12/5/15	+	6 hours.	0	+	Numbers of W. B. C. Majority well preserved. A few slightly irregular in outline.	Acid.	
21937	61	1/27/16	Partial resection of bladder.	21855	Carcinoma of bladder.	1/25/16	+	Immediate.	+++	+	0	Bacilli.	Small amount pus. Well preserved.	Acid.	B. typhosus and Streptococcus.
22029 Col'd.	37	2/16/16	Nephrectomy, left.	22029	Pyonephrosis, nephrolithiasis.	2/14/16	+	Immediate.	0	+	0	Non-motile rods.	Large amount pus. Well preserved.	Acid.	B. coli.
21990	9	3/1/16	Nephrectomy, right.	21935	Pyonephrosis.	2/24/16	+	Immediate.	+	+	0	Non-motile rods.	Large amount pus. Well preserved. Occasional slightly irregular cells. Same as above.	Acid.	Staphylococcus albus.
22578	34	10/20/16	Nephrolithotomy, right.	22587	Nephrolithiasis.	10/14/16	Right kidney.	Immediate.	+	+	0	Non-motile rods.	Small amount pus. Well preserved.	Acid.	No growth.
22497	55	10/23/16	Autopsy. No operation.	4902	Pyonephrosis, left.	10/19/16	+	Immediate.	0	+	0	Cocci.	Same as above.	Acid.	
22683	38	12/6/16	Nephrotomy, right.	22697	Nephrolithiasis.	10/20/16	+	Immediate.	0	0	0	Bacilli.	Well preserved.	Acid.	
22819	46	1/27/17	Nephrectomy, left.	22802	Nephrolithiasis, pyonephrosis.	12/6/16	+	1 hour.	+	+	0	0	Small amount pus. Well preserved.	Acid.	
F 64156	57	12/20/16	Nephrectomy, right.	22724	Hypernephroma.	1/27/17	+	Immediate.	0	0	0	Non-motile rods.	Large amount pus. Some broken cells.	Neut.	Staphylococcus albus.
Mrs. F	30	6/18/16	Nephrolithotomy.	Nephrolithiasis.	6/15/16	+	6 hours.	0	+	0	Urine not kept sterile.	Large amount pus. Well preserved.	No growth, right kidney.
21855	50	1/26/16	Nephrolithotomy, bilateral.	21850	Nephrolithiasis, bilateral.	1/26/16	+	Immediate.	0	0	0	0	Large amount pus. Majority well preserved. Same as above.	No growth from bladder.
								Right kidney. Left kidney.	Immediate.	+	0	0	0	Very few W. B. C. Many irregular. No marked degenerative forms in any specimen.	
22109	49	5/2/16	Nephrectomy, right.	22145	Hydronephrosis, chronic nephritis. Double kidney pelvis.	5/2/16	+	1 hour.	0	0	0	Bacilli.	Moderate amount pus. Majority slightly irregular in outline and no marked degeneration.	
22164 Col'd.	38	6/3/16	Pelvic puncture.	Autopsy 4718 6/9/16	Pelvic abscess, rupture into peritoneal cavity and bladder. General peritonitis.	6/5/16	+	Immediate.	0	0	0	0	Large amount pus. Well preserved.	Acid.	
22137	37	12/22/15	Cystostomy.	Chronic ulcerative cystitis.	12/12/15	+	8 hours.	+	++	0	Large amount pus. Majority well preserved. Occasional degenerated W. B. C. Considerable number show slightly irregular outline.	Acid.	B. coli.
						12/14/15	+	Immediate.	+++	+	0	Non-motile rods.		

Two cases of renal tuberculosis showing degeneration of leucocytes were reported by Micheli.

Lequeux (quoted by Micheli) found degeneration present in both tuberculous and non-tuberculous urines.

Kelly and Burnam were unable to substantiate the observations of Colombino.

Colombino demonstrated the tubercle bacillus in only six of his 20 tuberculous cases. Micheli did not find the tubercle bacillus in either of his cases. Moscou says the tubercle bacillus was found rarely in his series, but does not mention the exact percentage.

In our 11 cases of renal tuberculosis, the tubercle bacillus was demonstrated in 10. Unfortunately the other case did not show any leucocytic degeneration, nor were red blood cells seen in one examination.

Acid-fast bacilli have not been found in any case of non-tuberculous pyuria, although numerous smears have been examined carefully.

Our notes include 72 cases of pyuria, in 27 of which the possibility of tuberculosis could not be positively eliminated, and these cases have not been tabulated. The majority of these patients were not under observation long enough to be thoroughly studied.

The tables include 11 cases of renal tuberculosis, for which nephrectomy was performed, 15 cases of non-tuberculous pyuria in which the possibility of tuberculosis was definitely eliminated by operation or autopsy, and 20 cases in which there was no operation but the clinical picture and results of treatment rule out tuberculosis.

TABLE IV.

Type of case.	Operation + or 0.	Num- ber of cases.	Degeneration.	
			+	0
Tuberculosis of kidney	+	11	Marked in 6. Moderate in 1.	4
Nephrolithiasis	+	8	Variable but never marked, 2.	6
Pyonephrosis without stone	+	2	0	2
Hydronephrosis	+	1	Majority WBC. sl. irreg.	—
Hypernephroma	+	1	0	1
Carcinoma of bladder	+	1	0	1
Pelvic abscess with rupture into bladder	Autopsy	1	0	1
Cystitis, gonorrheal	0	4	0	4
Cystitis, general (B. coli)	0	6	0	6
Cystitis, general ulcerative	+	1	Moderate in some spe- cimens, others well preserved.	—
Cystitis, general with pyelitis	0	1	0	1
Cystitis, general ulcerative, with infected hydronephrosis	0	1	0	1
Pyelitis, acute	0	1	Marked.	—
Pyelitis and ureter stricture, bi- lateral	0	1	0	1
Pyelitis and ureter stricture, uni- lateral	0	1	0	1
Bladder ulcer	0	3	0	3
Trigonitis and urethritis	0	2	0	2

The voided urine from five patients contained well-preserved leucocytes, whereas in the catheterized specimens there were no leucocytes.

TECHNIQUE.

Colombino studied both fresh preparations from the cen-
trifugalized sediment and stained smears, but concluded that
the fresh unstained preparations were preferable, as in stained
smears irregularities of the cells can be produced artificially.
The fresh preparations consist of a drop of centrifugalized
sediment on a slide covered with a cover-glass and can be
examined with the high-dry lens or oil-immersion lens. Gold-
berg examined fresh preparations without a cover-glass in
order to eliminate a possible source of trauma to the leucocytes.

We have examined most of our specimens with and without
cover-glasses and in a blood-counting chamber, but have not
observed any cellular irregularities caused by the cover-glass.

The specimens of urine examined were usually obtained by
catheterization of the bladder or ureters, but numerous voided
specimens have also been examined. In women it is necessary
to obtain catheterized urine for a diagnosis of pyuria. Speci-
mens have been examined immediately and several hours
after collection. There is no evidence that the leucocytes
degenerate after standing for from 12 to 24 hours, although
we believe the specimen should be examined soon after collec-
tion. Some of the specimens have been centrifugalized and
others have not.

The culture work has been done in the Medical Bacterio-
logical Laboratory by Doctors Clark and Sydenstricker.

CONCLUSIONS.

Degenerated leucocytes in the urine are not pathognomonic
of tuberculosis of the urinary tract, but a marked degenera-
tion is strongly suggestive of this disease.

The absence of degeneration of leucocytes does not eliminate
tuberculosis.

The cytological study of the urine cannot replace the
demonstration of tubercle bacilli or animal inoculation as a
means of diagnosis; at best it offers presumptive evidence.

I wish to thank Dr. H. A. Kelly for permission to publish
these observations, and Doctors Hunner, Leonard, Holmes
and Richardson for their assistance and suggestions.

LITERATURE.

Colombino: Contribution à l'étude du diagnostic de la tuber-
culose de l'appareil urinaire, cytologie urinaire. Jour. d. mal. d.
organes génito-urinaires, 1906, XXIV, 81-103.
Goldberg: Die Form der Leukocyten im Harn bei Tuberculose
der Harnweg. Deutsche Med. Wehnschr., Leipz. u. Berl., 1909,
XXXV, 141.
Kelly and Burnam: Diseases of the Kidneys, Ureters and Blad-
der. Vol. II, p. 65.
Lequeux: Traité d'urologie, pp. 165 and 450.
Micheli: Sur la valeur de la dégénérescence leucocytaire (signe
de Colombino) pour le diagnostic rapide de la tuberculose uro-
génitale. Jour. d'urol. méd. et chir., Par., 1914-1915, VI, 409-418.
Moscou: Diagnostic de la tuberculose de l'appareil génito-
urinaire d'après l'examen microscopique des urines. Presse méd.,
1907, XII, 9.

THE ETHICS OF THE PRACTICE OF MEDICINE FROM THE JEWISH POINT OF VIEW.¹

By DR. HARRY FRIEDENWALD.

No people have laid greater emphasis upon the sacredness of life than have the Jews. The human being reflected the holiness of God, for "in the image of God made He man" (Gen. I, 27). But life itself, even the life of the lower animals, was held dear, for "the righteous man regardeth the life of his beast" (Prov. XII, 10). To care for one's health was regarded as a religious duty.

The people who looked upon life as sacred were naturally solicitous in their care of the sick. One of the highest duties was to visit the sick, and in the Talmud we read that this obligation extended equally to visiting the Gentile and the Jew. (Talmud, Gittin 61a.) This was in conformity with the verse "Thou shalt not abhor an Edomite, for he is thy brother; thou shalt not abhor an Egyptian, because thou wast a stranger in his land" (Deut. XXIII, 8). The tolerant spirit of the Jew was shown in his readiness to help the Gentile in distress.

Throughout Hebrew literature we find the most humane references to the sick. Thus in the *Sefer Hasidim* of R. Judah of Ratisbon (12-13th cent.) we read:

If a rich man and a poor man be sick and thou seest all the world going to see the rich man, go thou to the poor one, even though he be ignorant and unlectured Make no sign of visible disgust when thou meetest people afflicted with loathsome visible disease; for they are God's creatures, remember, and healthy as well as sick are all alike dependent upon him.²

The duty to treat the injured is expressed in Exodus (XXI, 18, 19): "And if men contend, and one smite the other with a stone or with his fist, and he die not, but keep his bed; if he rise again, and walk abroad upon his staff, then shall he that smote him be quit; only he shall pay for the loss of his time, and shall cause him to be thoroughly healed."³

This is not the occasion to discuss the theological dispute as to the propriety of any human interference in disease, looked upon as a visitation of God. Though the dispute was waged for a long time in Judaism and in Christianity, the practice of medicine won its proper position among the Jews at an early date. We are not surprised to learn that the Jews made great demands of the physician, that the ethical standards they set up for him were very high. Could less have been expected of those who followed the profession of Him who said: "I am the Lord that healeth thee" (Exodus, XV, 26).

¹ I desire to express my gratitude to Dr. E. N. Rabinowitz, The Johns Hopkins University, Baltimore, Dr. A. A. Neuman, Dropsie College, Philadelphia, and especially to Professor Alexander Marx, Jewish Theological Seminary, New York, for the valuable help they have rendered me in the preparation of this essay.

² See Zunz: *Jewish Moralists in "Hebrew Characteristics."* American Jewish Publication Society, New York, 1875, p. 22.

³ A curious version is found in the Vulgate and other translations: "That he make restitution for his work and for his expenses upon the physicians." (See Douay Version.)

It was regarded as proper that the physician should receive recompense for his service. Of course this was not to act as a hardship to the poor. We read that Abba (a leech and therefore belonging to a class that did not enjoy the same esteem as did the physician) had in his office a money-box into which those who received treatment would place what they desired to give. But no one could tell how much or how little each one paid. When a learned man came he would accept no payment, and if the patient was poor he would help him with a gift and refuse to accept any fee. (Talmud Taan. 21b.)

The physician was expected to treat his patients in a sympathetic and humane manner. This is beautifully shown in a passage in the Midrash, the ancient homiletical exegesis of the Thora:

Even when the physician sees that death is approaching, he still says to the patient "Eat this and abstain from that, drink this and not that," but he does not say "Your end is near," and it rebukes the prophet Isaiah in the name of King Hezekiah for telling him bluntly "Set thy house in order for thou shalt die and not live" (II Kings XX, 1).⁴

In the great code, the *Shulhan Aruch*, which Rabbi Joseph Caro⁵ wrote in the third quarter of the 16th century and which embodies rabbinic laws, we find an important chapter dealing with the rules governing the practice of the physician.⁶

TEXT OF RABBI JOSEPH CARO.

1. The Thora permits the physician to treat disease. It is a meritorious act to do so, under the general principle of saving a life in danger. One who refrains from doing so, sheds blood [*i. e.*, is guilty of sacrificing life]. Even if there is another who can treat the sick man, the physician dare not refuse his services, because it is not through the aid of every man that the patient has equal chances to be cured. Yet should no man occupy himself with medicine, unless he is well trained and there is no one better fitted than he in the place; otherwise, he is shedding blood. If one treats a patient without the approval of the court [official license] he is in duty bound to pay damages, even though he is an expert. And if he treats a patient with the approval of the court and errs and injures the patient, he is not responsible to the human court but he is not absolved from his obligations to the higher, the heavenly court. If he kills the patient through negligence and he becomes aware that he is guilty of unintentional murder, he goes into exile [as "the manslayer that kills any

⁴ This subject is taken up in detail by Preuss, *Virchow's Arch.*, CXXXVIII, 280.

⁵ R. Joseph Caro was born in Portugal in 1488 and died in Safed, Palestine, in 1575.

⁶ *Shulhan Aruch* Yorah Deah, 336.

person through error." See Numbers, XXXV, 9-34: Deut., XIX, 1-13.]⁷

2. A physician is prohibited from taking a fee for his expert knowledge or for instruction, but only for his pains and for the time he spends.

3. If one has drugs and his sick neighbor wishes to buy them, he is prohibited from raising the price higher than is

⁷ The responsibility of the physician is formulated in the Tosefta, an ancient collection of detailed statements of the traditional law. Tosefta (ed. Zuckermann), Gittin, IV, 6. A professional doctor, authorized by Beth Din, who has caused harm to his patient is free if the error was unconscious but guilty if it was knowingly committed, for the sake of the social order.

Ibid., Baba Kama, VI, 17: A professional doctor authorized by Beth Din, who has harmed his patient is free before a human tribunal, and his judgment is referred to Heaven.

Ibid., X, 11: A professional doctor authorized by Beth Din who has caused harm to his patient is free; if he has wounded him more than was necessary, he is guilty.

Ibid., Makkot, II, 5: A professional doctor authorized by Beth Din who has caused the death of a patient is exiled (to the cities of refuge). This holds true only if the doctor did just what was required; but if he has exceeded the limit and thereby caused death, he is not exiled because he is guilty wittingly. Nevertheless, he does not incur the penalty of death.

That the passages are not altogether consistent is quite apparent and Duran summarizes his exposition of these laws as follows: "If a physician authorized by Beth Din to practice caused harm to his patient, which other physicians discovered to be due to his error, then he is legally guilty of assault whether the error was committed consciously or unconsciously. If he caused death, he has the status of a murderer. But if he made no error in the nature of the treatment and was unsuccessful in carrying it out, then for the sake of the social order (*i. e.*, that the doctors should not give up their profession) he is acquitted by the human tribunal and his judgment is referred to Heaven; while, if he caused death, he is exiled. If, however, he exceeded the necessary measures, then he is guilty of assault or murder and must pay damages in the one case, and the penalty of death in the other event, if he was forewarned, or left to the vengeance of the 'redeemer,' if he was not warned." Duran, who was himself a physician, (Respona, Part II, No. 52), ends this paragraph with the pious wish: "And may God grant our portion to be among those who are successful in their profession and may He save us from errors, Amen."

It is here that Duran proceeds to draw the contrast between medical doctors and surgeons, thus: "It appears that by 'Rophe umman' is meant one who heals wounds with the work of his hands. If he commits an error consciously or unconsciously, he inflicts a bruise; if he uses a metallic instrument he causes death . . . but one who cures the sick with medicines, laxatives, drugs, baths, and resting is not called 'Rophe umman' but 'Rophe' and is not included in the former category. He cannot be sued for damages as he did not wound his patient. If such a physician commits an error and causes death or increases the suffering of his patient, he is free even before the judgment of Heaven, if his intentions were to cure and not to harm the patient. For he can judge but what his eyes see. But he must not rely upon his own experiments and reject the opinion of greater experts. If a doctor conducts himself rightly and properly, his Heavenly reward will be great, because his profession is a dangerous one and he must have exercised great caution." (This account of the Tosefta has been given me by Dr. A. A. Neuman.)

proper. Furthermore, if they agreed upon a high price because of the exigencies of the moment (for he was the only one who had these drugs) he may claim only their proper value. However, if the patient agreed to pay a large fee to a physician (for his services), he must pay it, because the physician sold his expert advice. The patient has no further redress.

Annotation by Rabbi Moses Isserles to Rabbi Joseph Caro:⁸ It is true, it is a duty incumbent (upon the physician) to treat (the patient). For it is commanded that everyone come to the help of one whose life is in danger. If, however, the performance of this duty falls to one who refuses to act without remuneration, the court cannot deprive him of his fee. Neither can it release those who obligated themselves from fulfilling this obligation. (This is based upon a quotation from Rabbi Jacob ben Asher on the authority of Rabbi Moses Nachmanidis.)⁹

In the writings of Jewish physicians of early and later mediæval times there are a number of references to medical ethics; some of these deserve consideration. An essay has recently appeared by Professor Ludwig Venetianer on Asaf Judæus, whom he describes as the oldest medical writer in Hebrew (Budapest, 1915).¹⁰ He shows that Asaf Judæus wrote various works on cosmography and medicine, and he gives evidence to prove that Asaf lived at the latest in the 7th century and in Mesopotamia. The words of admonition which Asaf and his colleague John spoke to their pupils and the oath which they required of them are of great interest to us:

Beware of causing death to anyone by administering the juices of poisonous roots. Do not administer to an adulterous wife an abortifacient drug. Let not the beauty of woman arouse in thee the passion of adultery. Divulge not any secret entrusted to thee and do no act of injury or of harm for any price. Do not close thy heart to mercy toward the poor and the needy. Say not of the good that it is evil, nor of the evil that it is good. Walk not in the path of sorcerers who raise enmity in marital couples through incantation, magic and witchcraft. Do not covet any possession as a reward for having aided in an act of infamy. In thy treatment do not apply the arts of the idolater, and place no trust in idols, for they are naught and are of no avail. On the contrary, ye must despise their servants; dead spirits are their idols without ability to help their lifeless images; how much can they avail the living human beings? Put thy trust in the Eternal, the God of Truth; He kills and He likewise brings to life; He punishes and He heals the wound; He gives to man understanding to be of help; He punishes in righteousness and justice, but He restores in love and in mercy; He makes plants of healing to grow up and he implants into the perfect heart the ability to heal, in order to make known His great grace and his wondrous works before great multitudes, so that all living may understand that He is the Creator and beside Him there is none who can help. The nations place their trust in idols who cannot help them in the hour of need, nor save them in their distress; thus their hope and their longings lead unto death. It is proper, therefore, that ye separate yourselves from them, that ye keep yourselves far removed from their idols

⁸ Rabbi Moses Isserles lived in Crakow from 1520-1572. His annotations are regarded as essential and as binding, especially by the Askenasic Jews.

⁹ The translation from the Shulhan Aruch has been prepared by Dr. Rabinowitz.

and that ye call upon the name of the Eternal, the living God, the God of the spirits of all flesh, in whose hand lies the power over the souls of all living and the spirits of all mankind, to kill or to bring to life; no one can escape from his might. Keep Him in mind at all times, seek Him in truth, rectitude, and perfection; then will all the works of your hands succeed. He will help you to be of aid to others and ye will be praised highly by all mankind; the people will forsake their idols for the service of the Eternal, for they will recognize that they had placed their trust in nought, that they had wearied themselves in vain in the service of gods which cannot be of help. Therefore be ye strong and not indolent, for great reward awaits your work. God will be with you, if ye are with him. If ye keep the covenant of your oath and if ye follow our instructions, then ye will be honored as saints in the eyes of all mankind who will say: "Happy the nation whose God is the Lord; the people whom he has chosen for his own inheritance." (Ps., XXXIII, 12).

Then the pupils answered and said:

Everything concerning which ye have admonished us, and everything which ye have commanded us, we shall heed, for it is the law of the Thora and it is our duty to obey it with pure heart, with whole soul and with all our strength and not to depart from it either to the right or to the left.

Thereupon they blessed the pupils in the name Almighty, the Creator of heaven and earth, and they continued to speak words of caution to their pupils and they said:

See the Eternal, His Holiness and His Thora are the witnesses that ye fear Him and that ye will not swerve from His laws but that ye will follow his commandments and that ye will not depart from the straight path, in order to gain profit from helping him who is lying in wait for the innocent soul, or from him who mixes poison to kill. Do not make known to anyone which plants are poisonous, nor give them to anyone. Allow no one to persuade you in any manner to produce disease in any one. Take heed lest ye cause any bodily deformity whatsoever and be not too much in haste to apply the knife. Do not apply cupping immediately but only when ye have considered and examined carefully two and three times, then only shall ye apply this remedy. Beware lest the spirit of pride come upon you and lest ye bear revengeful hate against any sick one. In your speech be upright and truthful, then will ye find grace in the eyes of God and among men will ye be regarded as honest, trustworthy and upright physicians.

One of the most remarkable statements bearing upon ethics of medical practice from the Jewish point of view is to be found in the "Aphorisms" or "Introduction into Medicine" of Isaac Judaeus, consisting of 50 articles.¹⁰ Isaac Judaeus (Abn Jacob Ishak ben Soleiman El-Israeli) is a name well known in medicine. He was born in Egypt about 830, lived in Mauretania and Cyrenaica (Northern Africa) and died about 932. The following is a translation of a number of the aphorisms:

(2) As the science of medicine is so extensive and the life of man too short to attain the whole, physicians of experience must be separated from the foolish, they must "purify themselves, make themselves white and be refined" (Daniel XII, 10), for by their constant study of literature and ceaseless investigation they distinguish themselves from the rest of mankind.

(3) The rapidity or slowness or hesitation in the work of an artisan depends upon the importance or unimportance or indifference of the object upon which he is working. He, who is busied in drilling openings in pearls must be very careful not to destroy the beauty of his work through haste. But it is different with him who is collecting the filth of the street. It is fitting that he who is engaged in the cure of human bodies (which are the most precious of all of the creations of this nether world) consider and examine carefully the diseases that may occur, and give his directions after mature deliberation and consideration so that he make no irreparable error. Therefore the sage (Mesue) says: "If you find a physician who is ready as soon as asked to give information about every disease and particularly to praise his own methods of treatment, you may regard him as a knave." The prince of physicians (Ibn Zoar) says: "I have never given a person a purge without having been anxious in my mind and having spent sleepless nights before and after."

(4) Just as the physician, according to what has just been said, should not be over hasty in acting, so he dare not be negligent or dilatory, for in the case of most diseases there is no time to be lost. He should, on the contrary, hold to the mean between these extremes and be neither too hasty and precipitate nor too tardy and negligent; in acute diseases he must think and act quickly because they are pressing.

(11) The physician does not bring about the cure, but he prepares and smoothes the way for nature; nature is the actual healer.

(15) The need of the physician is twofold, preserving health and curing disease; and the demand for the former is greater than for the latter; for it is better for man that he avoid becoming ill than that he become ill and be cured.

(17) The physician who promises to cure disease with certainty takes a serious responsibility upon himself. . . .

(21) If it is possible to bring about a cure by means of foods or healthful nourishment, then do not administer drugs because these, and especially the purging ones, are contrary to nature and are her enemies.

(23) Endeavor in thy treatment always to use the simple drugs, because it is easier for thee to acquire the knowledge of their action than that of the complicated ones.

(25) Never rely in treatment upon wonderworking cures, for these depend mostly upon ignorance and superstition.

(27) It is fitting to the profession of a physician that he should be moderate in eating—that he should not become a debaucher nor a glutton. It is a shame and a reproach, if he suffer from tedious illness, for then the people will say: "How should he who cannot cure himself, cure others?"

(28) Seal thy mouth to prophetic and self-evident expressions. What thou sayest should generally be stated as conditional.

(29) Suffer not thy mouth to condemn when something happens to a physician, for everyone has his evil day. Let thy deeds praise thee, and seek not thine honor in another's shame.

¹⁰ Published with German translation by David Kaufmann, in 1885.

(30) Make it thy special concern to visit and treat poor and needy patients, for in no way canst thou find more meritorious service.

(31) Try to ease the mind of the patient, encourage him to look forward to being cured, even if thou art not thyself convinced of it, for this will greatly strengthen his nature.

(38) When the patient does not follow thine injunctions or his servants and people do not promptly obey thine instructions or show thee the proper respect, it were better to give up the treatment.

(39) Fix the fee of thy patient when his disease is in its ascendancy and most severe, for as soon as he is cured he will forget what service thou hast rendered.

(40) The more thou demandest for thy service, the higher thou fixest the fee for thy treatment, the greater will they appear in the eyes of the people. Thine art will be looked upon as insignificant by those whom thou treatest for nothing.

(42) Do not visit thy patient too often and do not remain with him too long, unless the treatment of the disease demands it, for it is seeing the doctor anew that gives joy to the patient.

(43) Too large a practice confuses the judgment of the physician and causes him to give mistaken directions.

(46) Be concerned in the treatment of princes and the wealthy, for they will be liberal to thee with their means, will always praise thee and will be devoted to thee after their cure, while the common nobodies, when they are cured, will even hate thee when they think of the fee which thou hast taken from them (Prov. XXIII, 7).

(50) Excessive activity and effort diminishes the power of the physician and weakens his spirit, for he must constantly think and be concerned about each patient, hopeful for his recovery, and pray for him as though he were "one of his kin, that is near to him" (Lev. XXI, 2).

An interesting glimpse into the rules of medical conduct is given in the will of Judah ibn Tibbon, a famous Jewish scholar, translator and physician, who lived in Granada, Spain (1120-1190). The following is taken from the ethical will of Judah ibn Tibbon to his son:¹¹

My son, let thy countenance shine upon the sons of man; visit their sick, and let thy tongue be a cure to them; and if thou receivest payment from the rich, attend gratuitously upon the poor; and the Lord will requite thee, and give thee thy reward. Thus shalt thou find favour, grace, and good understanding, in the sight of God and man; thou wilt be honoured by high and low among Israel and the nations; thy good name will go forth far and near; thou wilt rejoice thy friends, and make thine enemies and adversaries jealous. Thou knowest already what is said in the Mibchar Hapeninim: "He who is desirous of having revenge on his enemies, should strive to improve himself to perfection." . . . My son, accustom thyself to examine the drugs and medicinal vegetables one day every week; and do not apply an article which thou dost not thoroughly understand . . . Why shouldst thou not be ashamed of thyself, and of the people, who all know that it is owing to thine intemperate diet that thou art sick every year? Indeed, there is no greater shame and disgrace than that of a physician to be ill from intemperance, one who is to mend others and cannot mend himself.

From the Responsa of Ibn Adret in the 13th century we cull the following: Asked whether a Jewish doctor may render obstetric service to a Christian woman, he replied that it was his duty to give his service to all who asked for it, to Jews and Christians alike and that his teacher, Nachmanides, had often treated Christian women.

I shall close this account with a reference to Amatus Lusitanus, eminent as a physician and medical writer, the vicissitudes of whose life portray those of his people during the middle ages. Born in 1511 in Portugal, he was reared as a Marrano (secret Jew). He was driven from his home by the inquisition and spent some time in Antwerp, Ferrara (where he taught medicine) and Rome and then settled in Ancona about 1549 where he resumed his family name and again professed Judaism. He acquired an extensive practice and was even called upon to treat Pope Julius III. But his persecution did not end and he was forced to migrate, finally reaching Salonica (about 1558) where he died of the plague in 1568.

He published works on medicine in the form of case histories, 100 in a volume, entitled "Centuries." The last of these, the seventh, written 1559, was published under the title "Curationum medicinalium centuries VII." It closes with the following oath or declaration, which gives expression to his views on the duties and ideals of the physician.

THE OATH OF AMATUS.

I swear by the Eternal God and by His ten most holy commandments which were given on Mount Sinai, through Moses as lawgiver, after the people had been freed from their bondage in Egypt, that I have never, at any time, done anything in these my treatments save what inviolate faith handed down to posterity; that I have never feigned anything, added anything or changed anything for the sake of gain: that I have always striven after this one thing, namely, that benefit might spread forth to mankind; that I have praised no one, and censured no one merely to indulge in private passions, unless zeal for truth demanded this. If I lie, may I incur the eternal wrath of God and His angel Raphael, and may nothing in the medical art succeed for me according to my desires. Concerning the remuneration, furthermore, which is commonly given to physicians, I have not been anxious for this, but I have treated many, not only zealously, but even without pay: and have unselfishly and unswervingly refused several rewards offered by many people; and have rather sought that the sick might, by my care and diligence, recover their lost health than that I might become richer by their liberality: all men have been considered equal by me of whatever religion they were, whether Hebrews, Christians, or the followers of the Moslem faith. As concerns loftiness of station, that has never been a matter of concern to me, and I have accorded the same care to the poor as to those born in exalted rank; I have never brought about sickness; in diagnosis I have always said what I thought to be true; I have unduly favored no venders of drugs, except perhaps those whom I

¹¹ Published by Edelman, London, 1852, pp. 8 and 14.

knew to surpass the others by reason of their skill in their art or because of their natural qualities of mind; in prescribing drugs I have exercised moderation in proportion as the powers of the sick man allowed; I have revealed to no one a secret entrusted to me; I have given no one a fatal draught; no woman has ever brought about an abortion by my aid; nothing base has been committed by me in any house where I was practising; in short, nothing has been done by me which might be considered unbecoming an excellent and famous physician. I have always held up to myself Hippocrates and Galen as examples worthy of being followed by me, and the records of many other excellent men in the medical art have not been scorned by me. In my method of studying I have been so eager that no task, however difficult, could lead me away from the reading of good authors, nor the loss of private fortune, nor frequent journeys, nor yet exile, which, as befits a philosopher, I have thus far borne with calm and invincible courage; and the many students which I have thus far had I have always considered my sons, and have taught them very frankly, and have urged them to strive to conduct themselves like good men. I have published my books on medical matters with no desire for profit, but I have had regard for this one thing, namely, that I might, in some measure, provide for the health of mankind. Whether I have succeeded in this I leave to the judgment of others. At all events I have held this always before me, and have given it chief place in my prayers. Given at Thessalonica, in the year of the world 5319 [1559].

A few years later Amatus died and one of his friends, the Marrano Flavio Jacopo de Evora, composed a memorial to him in beautiful Latin verses to the following effect:

He who so often recalled the breath well-nigh gone from the dying, and was, therefore, beloved by kings and peoples, lies far from the land of his birth, beneath the dust of Macedonia! (Graetz's History, English edition, Vol. IV, p. 610.)

Such were the ethical ideals of the Jewish physician in the middle ages. Surrounded by charlatanry, ignorance, fanaticism and bigotry, suffering cruel persecutions, driven from place to place, they held fast to these high ideals, for nothing lower would have been in accord with their traditions and their religion.

APPENDIX.

It would be tempting to include what is referred to in numerous accounts as the "Prayer of Maimonides." This appeared, in January, 1863 (*Allgemeine Zeitung des Judenthums*), in a German translation under the title: "Daily Prayer of a Physician Before Visiting His Patients, translated from a Hebrew manuscript of a celebrated Hebrew physician of the 12th century." It is a very lofty and beautiful prayer. It has been published and republished frequently and it is ascribed to Maimonides¹² or to "a distinguished Jewish physician of the 12th century," in such works on medical history

¹² An interesting analysis of this prayer is published by Kroner, in which he shows the harmony between it and the writings of Maimonides. (Ost und West, 1912, p. 745.)

as Haeser (1875, Vol. 1, page 837), and in biographies of Maimonides (such as Pagel's: *Maimuni als Medizin. Schriftsteller*, 1908, p. 244). Professor Gotthard Deutsch of Cincinnati has given an interesting account of the wanderings of this prayer and has shown that "it is the work of Marcus Herz, of Berlin (1747-1803), the friend and physician of Moses Mendelssohn, and was translated into Hebrew by Isaac Euchel, who published it in the Hebrew periodical, "Ha-Meassef, Vol. VI, pp. 242-244, 1790."¹³ On account of its intrinsic value, it is appended in an English translation.

DAILY PRAYER OF A PHYSICIAN.

Almighty God, Thou hast created the human body with infinite wisdom. Ten thousand times ten thousand organs hast Thou combined in it that act unceasingly and harmoniously to preserve the whole in all its beauty—the body which is the envelope of the immortal soul. They are ever acting in perfect order, agreement and accord. Yet, when the frailty of matter or the unbridling of passions deranges this order or interrupts this accord, then the forces clash and the body crumbles into the primal dust from which it came. Thou sendest to man diseases as beneficent messengers to foretell approaching danger and to urge him to avert it.

Thou hast blest Thine earth, Thy rivers and Thy mountains with healing substances; they enable Thy creatures to alleviate their sufferings and to heal their illnesses. Thou hast endowed man with the wisdom to relieve the suffering of his brother, to recognize his disorders, to extract the healing substances, to discover their powers and to prepare and to apply them to suit every ill. In Thine Eternal Providence Thou hast chosen me to watch over the life and health of Thy creatures. I am now about to apply myself to the duties of my profession. Support me, Almighty God, in these great labors that they may benefit mankind, for without Thy help not even the least thing will succeed.

Inspire me with love for my art and for Thy creatures. Do not allow thirst for profit, ambition for renown and admiration, to interfere with my profession, for these are the enemies of truth and of love for mankind and they can lead astray in the great task of attending to the welfare of Thy creatures. Preserve the strength of my body and of my soul that they ever be ready to cheerfully help and support rich and poor, good and bad, enemy as well as friend. In the sufferer let me see only the human being. Illumine my mind that it recognize what presents itself and that it may comprehend what is absent or hidden. Let it not fail to see what is visible, but do not permit it to arrogate to itself the power to see what cannot be seen, for delicate and indefinite are the bounds of the great art of caring for the lives and health of Thy creatures. Let me never be absent-minded. May no strange thoughts divert my attention at the bedside of the sick, or disturb my mind in its silent labors, for great and sacred are the thoughtful deliberations required to preserve the lives and health of Thy creatures.

¹³ American Israelite, March 19, 1908.

Grant that my patients have confidence in me and my art and follow my directions and my counsel. Remove from their midst all charlatans and the whole host of officious relatives and know-all nurses, cruel people who arrogantly frustrate the wisest purposes of our art and often lead Thy creatures to their death.

Should those who are wiser than I wish to improve and instruct me, let my soul gratefully follow their guidance; for vast is the extent of our art. Should conceited fools, however, censure me, then let love for my profession steel me against them, so that I remain steadfast without regard for age, for reputation, or for honor, because surrender would bring to Thy creatures sickness and death.

Imbue my soul with gentleness and calmness when older colleagues, proud of their age, wish to displace me or to scorn

me or disdainfully to teach me. May even this be of advantage to me, for they know many things of which I am ignorant, but let not their arrogance give me pain. For they are old and old age is not master of the passions. I also hope to attain old age upon this earth, before Thee, Almighty God!

Let me be contented in everything except in the great science of my profession. Never allow the thought to arise in me that I have attained to sufficient knowledge, but vouchsafe to me the strength, the leisure and the ambition ever to extend my knowledge. For art is great, but the mind of man is ever expanding.

Almighty God! Thou hast chosen me in Thy mercy to watch over the life and death of Thy creatures. I now apply myself to my profession. Support me in this great task so that it may benefit mankind, for without Thy help not even the least thing will succeed.

PALÆOPATHOLOGY.*†

By ARNOLD C. KLEBS, M. D., Washington, D. C.

Palæopathology is a term applied by Marc Armand Ruffer to recently developed methods of pathologic investigation in the realm of the very old. It is historical research because it endeavors to supply data in the evolution of mankind, not in the conventional sense, however, for its methods are those of direct and systematic observation. The adjective "pre-historic," used so often, would seem a misnomer, because the distinction of a history read in written records from one seen and studied in equally characteristic objects; chronologically determinable, is purely arbitrary and artificial and it would do no harm to drop it altogether.

The Greek prefix in "Palæopathology" may suggest a limitation of its scope to the era revealed to us in the fossilized forms of life. But such is not intended, although palæopathology has already found objects for research in this remote epoch. It is an American student, Professor Moodie, who is doing pioneer work in this field, by showing that the Mesozoon can yield most interesting pathologic and even bacteriologic specimens.^{9, 12} Another American investigator, Dr. Aleš Hrdlička, has developed intensively the palæopathological side in his numerous explorations and studies of the aborigines on this continent. The establishment by him of a very remarkable exhibition of palæopathologic specimens in San Diego, which is probably unique of its kind, is a great credit to scientific enterprise in this country.

These efforts, as well as the subject itself, deserve more general attention. The literature on the subject, especially the foreign one, being scattered in publications not readily accessible, a brief review may not be out of place at a time when opportunities for similar research are increasing.

We may justly regard Rudolf Virchow as the founder of palæopathology. His deep interest in archæology and anthropology made it inevitable that in the objects which came to his attention the pathological features should not escape him. Many reports of these observations of his will be found among his writings and his masterful descriptions still merit careful attention. Several of his pupils, as well as other investigators in Germany and France, have added reports of various specimens. In France and in this country (Robert Fletcher³) the subject of ancient trepanation has particularly attracted students. But to coordinate such isolated efforts, more material was needed and especially competent workers in the field, to supervise the excavations, to examine and order the material according to fixed standards. Such larger opportunities were offered only in recent years by the various scientific expeditions to Egypt and especially by the well organized archæological survey undertaken by the Egyptian Government in 1908 and 1909, previous to the artificial inundations caused by the closing of the Assuan dam. From this undertaking, carried out particularly by Drs. Marc Armand Ruffer, G. Elliot Smith and Wood Jones, dates the establishment of palæopathology as a special branch of research.

It is of the utmost importance that the age of the objects to be examined be clearly determined. Amateur explorers have too often ignored this. The exploring physician has to become an experienced anthropologist and archæologist or cooperate with such. The type of mummification, the posture of the body in the grave, its orientation, the geologic and cultural strata, objects of adornment, clothing and other fabrics, pottery and weapons, are some of the features successfully utilized for the dating of the remains. Without such circumstantial evidence the excavated pathologic specimens have very slight scientific value. Previous interferences with these burial grounds present problems well nigh insoluble. Just as artistic and architectural relics have suffered more from the

* A bibliography of the subject will be found at the end of this paper. The numbers in the text refer to it.

† Read before a meeting of The Johns Hopkins Hospital Historical Club, November 13, 1916.

hands of earlier "investigators" and collectors than from the wear and tear of time, so also the human remains have suffered by this neo-vandalism. Sometimes greed but more often plain ignorance is at the bottom of these devastations of precious material. But the archæologist and anthropologist will also have to learn to take notice of the objects showing pathologic features and preserve specimens which at first sight may seem to present only unimportant alterations.

The state of preservation of the objects from the earliest burial grounds, those of the Stone Age for instance, is usually such that the examination requires special precautions. Anyone who has ever assisted at an exhumation of a palæolithic or neolithic skeleton will readily appreciate this. Only very rarely can the bones, let alone the whole skeleton, be removed from the earth *in toto*. Everything is so brittle that the slightest touch will often destroy the structural outline. Successive layers of earth and rubbish have to be removed with great care from around the bones. When once laid bare, an artificial humidity must be maintained, otherwise the whole structure would pulverize into nothing. The form of such a skeleton can sometimes be preserved only by plaster casts or photographs. These difficulties obtain practically through the whole district of central and southern Europe, where the geologic history of living nature has been more intensively studied than anywhere else. Still, even here some interesting palæopathologic observations have been made.

So far, chiefly Egypt and Peru have furnished the more important specimens, but undoubtedly there are other regions yet unexplored, especially in the immense territories of Central Asia, Mesopotamia, the Irak and Central America, where important discoveries are to be expected. To make broad generalizations from the findings made so far would be premature, but it seems that there are some important differences between the pathology of those remote days and ours. Already we can faintly trace in these relics the primitive state when man's fate was sealed almost exclusively by injury or old age, gradually developing to that of the more complex nosology of our days. Sometimes we are even allowed to study the results of early therapeutic efforts. Some of the early surgical operations, trepanations for instance, of which we find such striking traces, propound riddles difficult to solve, others permit us to admire a great skill and the evidences of prolonged nursing care which we are astonished to encounter among primitive peoples. Again, in some specimens we find alterations which bear no resemblance whatever to such as are found to-day.

In order to give a concrete view of the possibilities of palæopathologic research I shall now review, under separate headings, some of the more recent findings illustrating the pathology of past ages.

BONE LESIONS.

The most frequent bone diseases among ancient peoples seems to have been *arthritis* and *osteitis deformans*. Wood Jones¹ includes within this term most of the hyperplastic bone changes which have been and still are described as rheumatic

or rheumatoid, since Adams in 1836 introduced the confusing term "rheumatic gout." Very justly Jones remarks that there is nothing to be gained by an etiologic nomenclature so long as we have so little definite knowledge about the causes. He therefore groups all of these changes under the term *osteitis*. Their clinical entity was established first by Haygarth in the 18th century ("nodosities of the joints") as distinct from gout and rheumatic fever. The latter, the acute, progressive, polyarticular arthritis was not found in ancient skeletons, and of gout only one case, a very interesting one, chemically determined as such, was seen in a mummy from an early Christian cemetery.

OSTEITIS DEFORMANS.*

Chiefly according to their localization the alterations encountered are distinguished as arthritis, spondylitis or simple osteitis. They are characterized by evidences of inflammation and the superposition of new bone tissue, often of fantastic proportions, regular stalactites, such as are rarely found nowadays. Sometimes there is some bulging and bending of the bones which ally these conditions to osteomalacia. The absence of ulcerative, necrotic defects can alone allow the important differentiation from syphilitic and tuberculous bone diseases. That this is not always easy will be shown later. Osteitis deformans must be considered the disease *par excellence* of the ancient Egyptian (Wood Jones) and probably that of all ancient peoples, to judge from reports of many other observers. In Egypt the evidences of its prevalence go back to predynastic periods. In the oldest times it appears that no single adult escaped some of its troublesome manifestations. Wood Jones is inclined to explain it on the basis of environmental causes, especially by the wet occupation in the Nile and subsequent exposure to the excessive heat and cold of the Egyptian climate. These same conditions existing to-day as then, while the frequency of the disease has distinctly diminished, rather tend to disprove Jones' theory. Neither can racial factors be made responsible, for the changes are found in a great variety of peoples. At any rate, a meaningless nomenclature will not hide our ignorance on the subject. Whether these processes can be explained, according to the tendency of the day, as due to infection is as conjectural as their specific allotment to tuberculosis, continuously insisted upon by Poncet on clinical grounds.

When we examine these bone changes, especially those of spondylitis, they present indeed striking resemblances to tuberculous bone disease. Closer investigation shows, however, the absence of distinct necrosis and medullary foci. Some resorption of bone may have taken place here and there, the intervertebral discs may have wasted under compression in kyphotic and lordotic deformation of the spinal column due to the unilateral fusion of the vertebræ. These are all features which, in spite of superficial resemblances, exclude the

* Sir James Paget restricted the use of this term to a disease which now bears his name but which is better described as chronic hypertrophic osteomalacia.

diagnosis of tuberculosis, at least so far as this term expresses our morphologic and bacteriologic notions of the disease. The spondylitic lesions seem always to precede the other localizations of the disease (metastases?). The lumbar column is most frequently affected and practically no archaic man seems to have been entirely exempt. In this connection, it is interesting to note that the derivative for "old age" in hieroglyphic writing is the picture of a deformed man (Ruffer). From the atlas to the coccyx no part of the spinal column (and as a matter of fact of the whole skeleton) was found unaffected. In one case from the third dynasty (*ca.* 3800 B. C.) and one from the Roman period (200 A. D.) the whole spinal column was one rigid bony mass. Pathologically it is the intensity of the process rather than anything else that distinguishes the ancient disease from the modern. Similar arthritic changes are found in all the other joints (somewhat less frequently in the knee) and it is notable that the accompanying hyperostoses are often more conspicuous in those parts of the bones which are at a distance from the joints. Roughened joint surfaces tending towards ankylosis are the rule and one sees rarely cases of the eburnation of the joint surfaces, so typical to-day. Humerus, ulna and femur present sometimes monstrous deformities, less so the phalanges of hands and feet where, however, the typical nodosities described by Bouchard (in connection with chronic dilatation of the stomach) were observed by Ruffer and Rietti.¹⁶ Whether the very peculiar deformations noted in the bones of the hip-joints of Peruvian origin by Hrdlička⁵ are essentially different, remains to be seen.

TUBERCULOSIS.

As already said, evidence of a marked prevalence of bone tuberculosis in the ancient Egyptian and also in the Peruvian seems to be lacking. The subject of pre-Columbian tuberculosis in North America cannot be profitably discussed on the basis of the available material. There is one carefully described case of supposed tuberculous spondylitis from a neolithic burial ground near Heidelberg (Bartels). But the vertebræ in the skeleton here examined were in such a state of disintegration that the conclusions arrived at do not seem altogether convincing. Poncet also described as tuberculous certain bone lesions found in a mummified monkey from a Theban cemetery (1000 B. C.). More convincing is the case of Potts' disease discovered by Smith and Ruffer¹⁶ at Philæ in the mummified body of a venerable priest of Amon, dating from the 21st dynasty. Here, not only the very pronounced kyphosis traceable to the necrosis of one or two vertebræ, but the former site of a psoas abscess could be demonstrated macroscopically and microscopically. The features revealed in this case led to the discovery of a whole series of others in the same neighborhood and to the hypothesis of an Egyptian health resort, a sort of sanatorium for the tuberculous, in charge of the servants of the "veiled deity"—a romantic supposition, but hardly provable.

Palæopathology gives only scant information about the possible prevalence of other forms of tuberculosis. Pleurai

adhesions were not infrequently met with and may point to pulmonary tuberculosis. This disease we have come to consider as the disease *par excellence* of civilization and especially of indoor civilization, and the theory of the increasing immunity against it among peoples longest accustomed to in-door conditions might well find strongest support or disproof from palæopathological research. The apparent infrequency of bone tuberculosis naturally does not dismiss the question about the incidence of other forms and it would be indeed erroneous to conclude that the ancient Egyptian was free from consumption which we encounter in early medical literature. The possibility that the manifestations of the disease may have altered within long epochs cannot be altogether disregarded, inasmuch as the great variability, at least in intensity, is well recognized.

OSTEOPOROSIS.

Under this name, structural alterations in cranial bones of young individuals, apparently without counterpart in modern pathologic experience, have been frequently encountered and described by observers in widely separated districts, as for instance Egypt and Peru. They seem to have nothing in common with those changes now found in bones of the very young or old, described by pathologists under the same heading or as *fragilitas ossium*, neither do they resemble the porosities one observes at certain stages in the hyperostotic accretions of bones in syphilitic disease. Two different forms seem discernible, one which is characterized by circumscribed patches of porous osteophytes, the other in which the porous condition prevails without marked osteophytic proliferation, but also without any evidence of bone necrosis. Strikingly characteristic, as pointed out by Hrdlička,⁵ is the localization of the patches in symmetrical regions of the skull and their confinement to those parts of the bone only which do not give attachment to muscles. Most frequently the osteophytic form is found on the roofs of the orbits (the only one described by the Egyptian observers); next in order come the frontal, parietal and occipital bone, and less frequently the wings of the sphenoid, parts of the temporals, and certain other bones of the base. There is no evidence that these formations have materially interfered with the well-being of the individuals affected. The findings so far do not allow the artificial construction of a clinical picture, distinguishing stages of active disease and recovery. As a matter of fact, it seems doubtful whether these findings allow us to speak of a disease at all, and conjecture about its toxic, nervous or what-not origin.

RACHITIS AND SYPHILIS.

Rickets, as defined pathologically to-day, does not seem to have been prevalent among archaic people. At least the characteristic lesions of the thoracic skeleton, the pelvis and the extremal bones (epiphyses) have not been found so far, with the possible exception of *coxa vara* conditions where, however, the bending of the femoral neck might be explained as a partial manifestation of the osteitis deformans which is

always present in these cases. Elliot Smith is inclined to consider certain distorted bones as evidence of rachitis. These mainly negative results cannot fail to astonish, because we have other evidences which suggest that rachitis did exist. I will only recall the frequent pictorial representation of deformed dwarfs and pygmies, also the bowlegged god *Bes* and the rachitic child on amulets of the Saitic-Persian period (Berlin Museum: von Oefele).

Syphilis, which we know to leave extensive and typical bone lesions, ought to be easily discernible in ancient bones, if the disease was at all prevalent. One remembers undoubtedly the reports which appeared at more or less regular intervals in our literature, about bones presumably pre-Columbian, exhibiting unmistakable signs of syphilis. Dr. D. S. Lamb,⁷ who is the custodian of a number of these interesting specimens in the Army Medical Museum at Washington, has reviewed the whole subject, so that I need not enter here into details. There is no doubt that some of the specimens (especially two skulls described as having belonged to prehistoric Aleutians of Chermoffsky in Alaska by their discoverers T. H. Bean and W. H. Dall) show typical syphilitic lesions; less convincing are those on some long bones and still less some so-called necroses which are undoubtedly postmortal changes. But the real difficulty with these findings—and Virchow called attention to it at the time—is that of dating them accurately. It is also a very precarious business to make a diagnosis from the alterations in some isolated bone. This is only possible when the lesion happens to be in an unmistakably typical stage. The great bone defects caused by the breaking through of medullary gummata, especially in the cranial bones, without noticeable hyperostosis, are very characteristic but error has to be guarded against, for small gnawing animals are known to produce very similar destructions in the buried bones (Virchow, G. Elliot Smith). Really pathognomonic in dry flat bones Virchow considers only those typical marks left by the cicatrization of a gummous peripheral osteitis, a condition first described by Brandi (1723-1765) as *caries sicca*. Traumatic or simple osteitic or osteomyelitic processes (especially those observed on the skulls of people who customarily carry burdens on their heads) may simulate conditions of syphilitic origin but never this *caries sicca*. Smith lays great stress on the corroborative value of changes found in the teeth. At any rate we may safely conclude that the whole subject of the pre-Columbian origin of syphilis is still *sub judice* and that from careful palæopathological research in the future, more than from anything else, a solution may be expected.

OTHER BONE LESIONS.

The teeth of the ancient Egyptians, like those of archaic people generally, are usually found in a state of excellent preservation. The attrition affects evenly the biting edges and surfaces and there is practically no deposit of tartar. In part this is probably due to a coarser kind of food than the one we are accustomed to. Gradually, however, conditions change to those closely approaching ours, as evidenced in the

skulls from later burial grounds. Here we find all the reminders of painful days in the form of dental caries, periodontitis and suppuration. Curiously enough no evidence of dentistry is found, not even that of tooth-pulling. Only one artificial tooth was seen and the gold wires wound around some teeth, claimed to be some orthodontal device, are now regarded as mere objects of feminine, or perhaps, male coquetry. Of interest is also a case of great hypertrophy of the middle turbinated bone with complete occlusion of the nasal passage (Ruffer). We have records only of few bone tumors. Hrdlička mentions the frequent occurrence of small osteomata in the auditory meatus and Ruffer¹⁷ described a larger tumor, probably an osteosarcoma, of the pelvis (250 A. D. Roman).

INJURIES, FRACTURES AND DISLOCATIONS (Sepsis).

The evidences of trepanations on skulls of ancient or primitive peoples have attracted probably the most widespread attention. A surplus of newer material precludes its discussion here, though its real meaning is not yet clear and ought to offer an interesting field for further research.²

The effects of injuries, whether accidental or purposive (battles, executions, etc.) can be observed in ancient bones in great variety. The Egyptian findings analyzed by Jones¹ and compared with modern conditions, as illustrated by the reports of the out-patient departments of hospitals in New York and London, form an interesting commentary on sociologic treatises, but it would lead too far to enter into this aspect here. Two facts seem to stand out prominently in the whole series: the almost entire absence of sepsis and a very pronounced tendency to natural repair. But some fractured bones had to be set artificially and a study of some of the healed fractures reveals a very high degree of skill, the variations of which can be traced in the several cultural epochs. The ancient bone-setter like the modern, saw his ideal in the avoidance of any deformity and the shortening of limbs, and we can verify his success in some of the healed bones by a comparison with the corresponding bone of the same skeleton. Of course great deformity and then always an abundant hyperplasia of bony tissue, as observed in fractured limbs of animals, are also found in the human remains, but this is by no means the rule. From the 5th dynasty on, we learn that splints were applied in cases of fracture, and some were found still *in situ* on the mummies. But we also know that other mechanical appliances must have been employed for the treatment of fractures when splints were not applicable and, in this direction, some of the findings corroborate directly the information we have from the literature. The collection of ancient surgery, based on the Hippocratic treatise on joints and commented upon by Appolonius of Kitium (1st century B. C.) is preserved in a precious illustrated Greek codex of the 10th century in Florence. It inspired several surgical works of the 16th century (Guido Guidi, Rabelais, Ambroise Paré *et al.*). In this collection we can see some of these ingenious appliances as used by the Greeks but very likely employed long before by the Egyptians.

DISEASES OF THE SOFT TISSUES.

As Ruffer¹⁴ has pointed out, the tissues of those bodies which were simply buried in the sterile, dry sand of Egypt, with or without the addition of salt, are the ones best suited for microscopic examination. The Egyptian undertaker, the *paraschist*, embalmed the bodies without the slightest regard to the interests of future investigators. He usually managed to destroy or remove all the internal organs, so that bodies, from the periods when his art was particularly flourishing, *i. e.*, the New Empire, furnish only the scantest material. None the less interesting records have been obtained by the special methods devised by Ruffer and his associates. I shall refer, however, only to a few of the more striking findings, especially to that of the discovery of calcified ova of the *schistosoma hæmatobium* and the arterial lesions.

Bilharziosis is still one of the most distressing and destructive diseases in Egypt and its demonstration in those remote periods offers, therefore, a subject of the greatest interest. The disease can very probably be identified with the *âââ* disease of the Ebers and Brugsch papyri, in which it is stated that it was caused by the worm *Nelta*. Now, as Pfister has shown, the probability of this identification is greater than that also attempted—with Egyptian chlorosis, an affection due to the activities of the nematode *Ankylostoma duodenalis*. Two reasons speak for it: First, the trematode causing bilharziosis is somewhat larger than the ankylostoma and secondly, the most striking symptoms of bilharziosis, the hæmaturia and the typical local manifestation (tumefaction of the penis) would naturally have led to the introduction of a pictorial phallus into the hieroglyphic determinative for the *âââ* disease (surely not so much the sexual impotence subsequent to ankylostomiasis, as has been advanced by Joachim).

The arterial lesions found have led to some interesting considerations.*

Most important among these are the evidences of atheroma. Shattock initiated the investigations by examining microscopically the aorta of King Minephthah (*ca.* 1350 B. C.) in 1909 and very soon after Ruffer¹⁵ evolved his excellent technic with which he searched a great number of mummies from the 18th to the 27th dynasty (1580-527 B. C.) and the time of the Persian Conquest (500 B. C.). The fact brought out by these investigations is the astonishing frequency of arteriosclerosis and the extent it reached in some individual cases. Rarely was the condition absent in older individuals. In some cases Ruffer found the arteries transformed into rigid "bony" tubes down to their minute ramifications. After decalcification and staining (Van Gieson) he obtained very interesting sections in which the course of the disease could be

studied almost as well as in a fresh specimen. Nothing in particular distinguished the histological findings from those observed to-day, but it is highly interesting that the arterial coats and the annular fibers were still clearly to be distinguished in these 3000-year-old specimens.

In view of the many modern speculations regarding the etiology of arteriosclerosis, it may be of interest to consider the question in the light of these venerable testimonials. Unfortunately, we cannot expect any illumination about blood pressure, a subject to-day occupying the center of the stage. Tobacco and syphilis we also have to exclude. The strenuousness of modern existence may or may not have had its counterpart in Egyptian life and Ruffer remarks very pointedly that we certainly cannot complain of overwork when we compare our activities with those of our ancestors. Meat diet and luxury, another presumed cause, probably existed more or less in all those Egyptian epochs, although meat was surely not the main article of food, as is to be seen in contemporaneous pictures of feasts in which vegetables always abound. Ruffer also found arteriosclerosis equally prevalent among the high-living priests and priestesses of ancient Deir el-Bahari as among young, modern Egyptians who eat meat but rarely. Neither can strenuous muscular exercise have been a causative factor in these same priests who were not likely to indulge in sports or hard manual work. There remains alcohol! When we remember Herodotus' report about the obligatory drunkenness in deliberative assemblies of the Persian legislators and similar references to vinous habits in Egyptian documents, we cannot adduce these facts for an etiologic comparison with modern conditions until prohibition has become a more solidly established institution. It might, however, help those who do not believe in the responsibilities of alcohol in this matter, to know that Ruffer examined the bodies of a number of Mussulman pilgrims who never had touched a drop of alcohol and found arteriosclerosis very frequently.*

Palæopathology is only in its very beginnings. The comparative scantiness of facts so far brought out and the difficulties of the research ought not to hinder its energetic pursuit. In the concatenation of specialized scientific inquiries it forms a precious link that well merits more widespread attention. It must be recognized that injury and disease have played an important part in the history of mankind. We need only consider what definite influence they exert in our individual lives, what profound social upheavals were brought about through the incidence of epidemics, less perceptibly perhaps but none the less strongly, through widespread chronic ailments, through professional diseases, how whole districts and countries were forsaken because disease made them uninhabitable, how diseases affecting early childhood and others producing sterility led to the gradual extinction of whole peoples. And also, as regards the microorganisms that we

* In passing it may be mentioned that examination has shown that the blood-vessels of some mummies had been injected with some substance not yet identified, but surely not bitumen. Further investigations on this subject may throw suggestive sidelights on the physiologic knowledge of the paraschists. The existence of aneurysm was suggested by the finding of one large opening at the base of one skull, due most likely to pressure erosion from an aneurysm of the internal carotid artery.

* For completeness' sake I must add that Ruffer discovered, in one mummy of the 20th dynasty, a skin eruption resembling microscopically and macroscopically that of variola, and that the detection in other cases of a hypertrophy of the spleen suggested the existence of malaria in those times.

make responsible for so large a share in our physical troubles, must it not be assumed that they also traverse evolutionary stages in their fight for existence in the same way as other forms of living substance? We may find evidence of varying virulence, of their producing in one epoch recognizable though negligible diseases, in the other disastrous calamities. For the grasp of such problems, the study of disease as it appears to us now does not suffice, the traces left during immense periods of time have to be taken into account and it is just in such questions, not approachable by other methods, that palæopathology in time to come may furnish important solutions.

The search for evidences of a primitive therapeusis may bring forth material which may throw a light on the earliest origins of medicine and on those very actual questions about the spontaneous, local origin or the spread of culture over the earth, from one particularly advanced center. One of the pioneers in palæopathologic research, Dr. G. Elliot Smith, ardently defends the latter alternative. He holds that all evidence of culture in the various lands of the earth, no matter how far distant they may be from each other, can be traced to the direct influence of emissaries from the great civilization built up in Egypt between 4000 and 900 B. C. The theory is based on some striking resemblances of certain rather bizarre cultural features (the so-called heliolithic culture-complex: suncult, mummification, huge buildings, tattooing of the chin, svastika emblem, etc.) in widely separated districts. These resemblances are indeed striking and forcibly suggest an interrelation of these people during some remote epoch, but they hardly justify the summary denial of the possibility of the spontaneous, independent rise of a primitive culture, based on the innate tendency of man to improve his surroundings, to avoid or alleviate suffering or to correct physical defects. This must be considered as due to instinctive efforts, to an "*a priori synthesis*" in William James' sense, which can be observed among all primitive peoples, even among animals to a certain degree, efforts which necessarily must resemble each other somewhat; such as we should probably find among peoples of some other planet beyond the possibility of receiving suggestions from Egypt or elsewhere. Although "originality is certainly the rarest thing in this world" [B. Laufer; Jade, 1912, p. 5], and although in a tolerably advanced stage of civilization it will be almost impossible to distinguish clearly between what is original and what is borrowed in medical practice, anything that will make us acquainted with the early rise and evolution of therapeutic procedures may carry valuable lessons. This is a side-issue of palæopathologic research, but not the least interesting one.

BIBLIOGRAPHY.

[References to the older palæopathological literature are cited in several of the articles in this list.]

1. Egypt, Ministry of Finance, Survey Department: The archaeological survey of Nubia. Report for 1907-1908. Cairo, 1910. 2 vols. text and plates. Contains: G. Elliot Smith and F. Wood Jones' report on human remains.

- Bulletin 2. (1907-1908.) Cairo, 1908: G. Elliot Smith and F. Wood Jones: Anatomical and pathological reports. (Illustrated.)
2. Fletcher, Robert: On prehistoric trephining and cranial amulets. N. Am. Ethnol. Washington, 1882, V. (Illustrated.)
3. Hrdlička, Aleš: Report on an additional collection of skeletal remains from Arkansas and Louisiana. J. Acad. Nat. Sc., 1909, XIV. (Illustrated.)
4. Hrdlička, Aleš: Some results of recent anthropological exploration in Peru. Smithsonian Misc. Collection. 1911, LVI, No. 16. (Illustrated.) [1st expedition.]
5. Hrdlička, Aleš: Anthropological work in Peru in 1913, with notes on the pathology of the ancient Peruvians. Smithsonian Misc. Collection. 1914, LXI, 1-69 of No. 18. (Illustrated.) [2d expedition.]
6. Jones, F. Wood: See above under "Egypt."
7. Lamb, D. S.: Pre-Columbian syphilis. Proceedings Am. Anat., 1898, X, 63 [cites the earlier American and European literature on the subject].
8. Mair, W.: On the lipoids of ancient Egyptian brains. J. Path. & Bact., 1913, XVIII, 179 [Reviews previous work on subject by W. A. Schmidt, 1907-1908].
9. Moodie, Roy L.: Mesozoic pathology and bacteriology. Science, 1916, n. s. XLIII, 425-426.
10. Moodie, Roy L.: Two caudal vertebrae of a sauropodous dinosaur exhibiting a pathological lesion. Am. J. of Science, 1916, XLI, 530. (Illustrated.)
11. Moodie, Roy L.: Bacteriologic and pathologic evidences in past geologic ages. Trans. Chicago Path. Soc., 1916, 84-88. [Gives previous literature beginning with work of B. Renault, 1899-1900].
12. Moodie, Roy L.: The structure and growth of the plesiosaurian propodial. J. of Morphology, 1916, XXVII, 401, 1 plate. (Illustrated.)
13. Raymond, Paul: Les maladies de nos ancêtres à l'âge de la pierre. Aesculape, Paris, 1912, III, 121. (Illustrated.)
14. Ruffer, M. A.: Remarks on the histology and pathologic anatomy of Egyptian mummies. Cairo Scientif. Journal, 1910, IV. (Illustrated.) [Microscopic demonstration in Cairo Sc. Soc., Dec., 1908.]
15. Ruffer, M. A.: On arterial lesions found in Egyptian mummies. 1580 B. C.-525 A. D. J. Path. & Bact., 1910, XV, 453. (Illustrated.)
16. Ruffer, M. A. and Rietti, A.: On osseous lesions in ancient Egyptians. J. Path. & Bact., 1911-12, XVI, 440. (Illustrated.)
17. Ruffer, M. A. and Willmore, J. G.: Studies in palæopathology. Note on a tumor of the pelvis dating from Roman times (250 A.D.) and found in Egypt. J. Path. & Bact., 1914, XVIII, 480. (Illustrated.)
18. Smith, G. Elliot: See also above under "Egypt."
19. Smith, G. Elliot and Ruffer, M. A.: Pott'sche Krankheit an einer ägyptischen Mumie aus der Zeit der 21. Dynastie (um 1000 v. Chr.). Ztschr. histor. Biolog. d. Krankheitserreger, Giessen, 1910. Heft 3. (1 plate.)
20. Smith, G. Elliot: On the significance of the geographic distribution of the practice of mummification. A study of the migration and the spread of certain customs and beliefs. Manchester Memoirs. Manchester. 1915, LIX. (Illustrated.)

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ABSTRACTS OF PAPERS

Representing Work Done in The Johns Hopkins Hospital, but Published or to be Published Elsewhere than in the Bulletin.
Prepared by the Authors.

A COMPARISON OF THE PERMANENCE OF FREE TRANSPLANTS OF BONE AND CARTILAGE. AN EXPERIMENTAL STUDY.

By JOHN STAIGE DAVIS, M. D., F. A. C. S., Baltimore, Md.

(Abstract from Ann. of Surg., 1917, Feb., p. 171.)

Introduction.—The appearance of a number of clinical papers advocating the transplantation of bone for the relief of saddle nose has interested me, because I had come to the conclusion that cartilage was the best material to use in such cases. As there seemed some difference of opinion as to the relative stability of bone and cartilage transplants, I carried out the following procedures on dogs, in order to clear the matter up, at least from an experimental standpoint.

In order to produce conditions which would be somewhat similar to those in actual clinical practice, I transplanted the cartilage and bone, each 2 cm. long, so that one extremity of the transplant was in close contact with a denuded portion of a membranous bone, while the remaining portion extended into the soft parts. Autotransplants only were used.

EXPERIMENTS.—Group 1. Transplantation of cartilage with its perichondrium intact, and rib without periosteum.—Six experiments. Specimens were examined after 24, 25, 85, 223, 576 and 582 days. In each the cartilage was found apparently intact, and 2 cm. in length. After 24 and 25 days there was little change in the length of the bone, although beginning absorption was noted. In the 85-day specimen there was a somewhat dense outgrowth of bone from the skull about the impinging portion of the transplant. This appeared rather excessive, when compared with that in the other specimens, and might have been caused by a slight localized infection. There was marked evidence of absorption, although the bone was still 2 cm. in length. After 223 days no bone could be found, either by X-ray or by dissection. In the 576-day specimen a very small irregular spicule of bone was found projecting from the skull. It measured 2 mm. in length and breadth, and 1 mm. in thickness. In the 582-day specimen an irregular spicule of bone, 0.5 mm. long, projected from the parietal bone.

This group seems to show that under the same conditions transplanted cartilage and spongy rib bone behave quite differently. The cartilage retains its original size, while the bone in the shortest experiment shows beginning absorption, and this progresses as time goes on. It is difficult to say why the bone in the 223-day experiment should have disappeared, while evidences remained of the transplant in experiments observed for more than twice that length of time.

Group 2. Cartilage with one-half of its perichondrium, (lengthwise), and rib without periosteum.—Four experiments. Specimens were examined after 44, 125, 374 and 505 days. In each the cartilage was found to be the same length as when transplanted. After 44 days the bone was a scant 2 cm. long

and showed evidences of absorption. After 125 days the bone was 1 cm. long, very thin and nearly absorbed. After 374 days only a thin spicule of bone, 8 x 2 mm., remained. After 505 days a thin fragment, 7 x 2 mm., remained.

Group 3. Cartilage without perichondrium, and rib without periosteum.—Two experiments. Specimens examined after 165 and 332 days. In both the cartilage was found to be 2 cm. long and apparently intact. In the 165-day specimen the bone had disappeared. After 332 days the bone was thin and flexible, and measured 7 x 1 mm.

These groups again emphasize the tendency of bone to be absorbed and of cartilage to retain its original length and thickness, even though partially or wholly denuded of its perichondrium. It is impossible to say why one of the rib transplants had disappeared in 165 days, while thin fragments of bone, showing all the signs of degeneration, were found 332, 374 and 505 days after transplantation.

Group 4. Cartilage without perichondrium, and rib with strip of periosteum.—Four experiments. Specimens were examined after 13, 26, 49 and 56 days. The cartilage remained unchanged in each. After 13 days there was no change in the size of the bone. In the 26- and 56-day specimens the bone was found to be 1.6 cm. long, and in the 48-day specimen it was 1.4 cm. long.

This group again shows the tendency of bone to absorb, in spite of the presence of undisturbed periosteum, and the cartilage to be unchanged, even though the perichondrium is removed.

Group 5. A section of fibula, with periosteum, and a similar section without periosteum, were transplanted as in previous experiments.—Three experiments. The sections of fibula to be compared were of equal length, and varied between 1.4 and 1.8 cm. in the different experiments. Specimens were examined after 305, 328 and 388 days. In each the section of fibula without periosteum had been absorbed. In the 305-day experiment the section of fibula with periosteum, which was originally 1.8 cm. long, measured 5 mm. long by 1 mm. at its widest, and was thin, irregular and flexible. In the 328-day experiment the transplant, which was covered with periosteum and originally was 1.75 cm. long, measured 8 x 1 mm., and was thin and flexible. After 388 days the fibula, covered with periosteum, which was originally 1.4 cm. long, measured 7 x 1 mm., and was thin and flexible.

This group shows that the hard bone of the fibula is absorbed, as well as the more spongy bone of the rib. It also confirms experiments previously reported, which showed that a bone covered with periosteum is more resistant to absorption than denuded bone, but that in time it also will be absorbed.

Remarks.—It has been often demonstrated that free bone, either with or without periosteum, when transplanted into soft parts, without any particular function, will eventually be absorbed. From these experiments this also seems to apply to

free bone transplants with one end in contact with denuded bone, as in no instance, where any considerable time had elapsed, was the transplant found holding its own against absorptive processes. In the experiment of longest duration only a tiny spicule of bone remained projecting from the parietal bone, and it is obvious that this remaining portion would have been insufficient had the original transplant been used as a supporting framework.

The cartilage in each experiment showed no signs of absorption and was normal in appearance, even when entirely denuded of perichondrium. In no instance was there any increase in the length of the cartilage.

The healing was reactionless, and the cartilage did not act as a foreign body. The measurements of the cartilage differed very little, if at all, from those taken at the time of transplantation. On section the cartilage appeared normal and seemed well nourished.

Conclusion.—These experiments show that transplants of free cartilage were unchanged during the length of time under observation, while free bone transplants under exactly the same conditions had either disappeared, or showed marked degenerative processes.

THE SIGNIFICANCE OF THE LUNULA OF THE NAIL.

By MONTROSE T. BURROWS, M. D.

(From the Department of Pathology, The Johns Hopkins Hospital and University, Baltimore, Md.)

(Abstract of article in The Anatomical Record, 1917, XII, No. 1.)

The nail is one of a few of the parts of the body which continues to grow throughout the whole life of the individual. In connection with the work on the mechanism of the cellular growth in the tissue culture, the author has undertaken a more careful study of this organ, hoping in the finer details of its structural peculiarities to find something of further importance for the better understanding of the conditions which regulate the growth of cells and tissues in the organism.

During the early part of this study the author has noted certain peculiarities in the structures of the lunular portions of the nail which, as far as he has been able to ascertain, give for the first time a definite explanation for the opacity of this region. The matrix throughout the lunular area does not adhere tightly to the underlying connective tissue, but lies merely in contact with these underlying structures, so that throughout this whole region possible reflecting surfaces are formed. In the outer portions of the nail the matrix is firmly attached to the underlying connective tissue. The connective tissue in this outer region is richly supplied with capillaries. The connective-tissue fibrils pass either directly from within outwards or obliquely outwards to end in and become attached to the basement membrane or the border of the cells of the matrix. Throughout the region of the lunula they take a quite different course. At the border of the matrix they run parallel to it; here they form a thin, dense layer or membrane. The connective tissue of this region contains few capillaries. These are in large part arranged in a network within and on the surface of this thin superficial connective tissue membrane.

In the modern textbooks of anatomy the opacity of the lunula has been ascribed to a peculiar opacity of the nail proper or of its matrix in this region. We have studied carefully by transmitted light many nails that have been removed together with their matrix. In no case, including a large majority of those nails which had been previously fixed and hardened, has the part of the nail corresponding to the lunula been found to be more opaque than other parts of the nail; quite to the contrary, it has been found to be more translucent.

Again, we have studied carefully a possible relation between the decrease in the number of capillaries in the connective tissue of the region of the lunula and the opacity in this region. These studies have yielded, however, little evidence that would indicate any such relation. First, it has been found that the change in the density of the capillary bed of the outer portion of the nail to that of the lunular portion at the distal margin of the lunula is never as abrupt as the boundary line of the lunula demands. Further proof against this peculiarity playing any important rôle in conditioning the opacity is given by comparing the appearance of the lunular areas with a portion of the body from which the blood has been removed by pressure. The lunula has a definite opacity, whereas that portion of the body from which the blood has been removed has a greyish translucence.

In absence of other possibilities, the author has been led to believe, therefore, that the lunular opacity is the result of a reflection of the light at the surfaces of the junction of the matrix and the connective tissue of this portion of the nail. In the outer portion of the nail where the matrix adheres closely to the underlying connective tissue the light is transmitted directly to the capillary bed giving it a characteristic pink color; while in the region of the lunula the well-formed non-adherent surfaces of both the connective tissue and the matrix reflect the light. More direct proof of this assertion may be readily obtained by pulling a portion of the body of a living nail loose from the connective tissue, thus forming such a surface in this region. During the past few weeks the author has been performing work which has led to the production of this injury. In every instance, in which it has occurred, the detached portion has shown an opacity quite indistinguishable from the opacity of the lunula of the same finger. It is of interest, however, that unless the injury is extensive the nail will again, after a few hours, become adherent and assume its former pink color.

The decrease in the capillary bed of the lunular area has been described (Poirier and Charpy, *Traité d'anat. hum.*, Paris, 1901). No one, on the other hand, so far as the author has been able to determine, has described the peculiarity of the adhesion between the matrix and the connective tissue in this region, or the relation of the peculiarity in structure to the lunular opacity. It will be of further interest to ascertain whether many of the pathological opacities of the nail are not the result of similar changes,* and to study more carefully the

* This explanation for these opacities has already been suggested by several different authors.

conditions which lead to the adhesion of the matrix in the outer portion as contrasted with that of the lunular zone, and the general changes in the connective tissue and in the arrangement and density of the capillaries in these two regions. In the analysis of these latter conditions, we believe, we shall find many important facts related to the nature of the mechanisms of growth and differentiation of the tissue cells.

THE TISSUE CULTURE IN CANCER.

By MONTROSE T. BURROWS, M. D.

(From the Pathological Laboratory, The Johns Hopkins Hospital and University, Baltimore, Md.)

(Abstract of paper delivered before the Second Pan-American Scientific Congress, Washington, January 6, 1916.)

(To be published in Trans. Second Pan-American Scientific Congress, 1917.)

Cancer considered in its general aspects is a condition, although unique, which must be understood only by the use of those same methods by which we are eventually to understand normal and other pathological processes. The important problem in pathology and in biology is the structure and metabolism of normal body cells. The question in cancer is whether the cancer cell is a normal cell responding to a peculiar environment or whether it is a cell whose metabolism is such that it can grow in an environment where other cells cannot show these changes.

At one time it was supposed that the cycle of the life of the organism was the cycle of the life of the cell. At the present time, however, this particular view has been largely discarded and it is now held that not only is the body controlled by its cells, but that the cells are likewise controlled by the body. There is a mutual interrelation between the whole and its minute parts. Each and every activity of the cell is a response on its part to some external stimulus. Each and every activity of the whole is the result of the coordinated activity of its parts. The cessation of the growth of many cells at maturity does not represent a loss of the property of these cells to proliferate, but is the result of some kind of a change either in the organization of the cell or in the parts about it.

Although it has been assumed that this peculiar type of regulation of growth and other changes in the body cells is the result of peculiarities of their structure and metabolism, and that it must be solved by direct analysis of the mechanisms peculiar to each of the various activities of these cells, up to the time of the development of the tissue culture method no means for such direct analysis had been devised. The tissue culture method has become important in cancer as in the study of normal and other pathological processes in that it allows one to study directly the reactions of these various cells in a restricted and analysable environment.

During the last few years the author has studied by this method several different kinds of normal and cancer cells. Through this study he has been able to demonstrate directly that the normal cells of the organism are essentially fluid systems and that the organization peculiar to their various activities, such as growth, movement, differentiation, function,

etc., are differential surface tension phenomena, regulated by the organization of the environment and the peculiar properties of certain of the substances formed in their oxidation reactions. The organization peculiar for each of these activities is not a cellular but a tissue organization. Thus it is seen how these cells may, under the influence of changes in their environment, undergo changes in form and activity.

A further careful study of oxidation in these cells has been made. Oxidation in these cells is a simple, incomplete, chemical reaction. CO_2 and another or other substances are formed. Certain of these compounds formed are insoluble in the circulating body fluids, serum, salt solution, etc., but soluble in various body colloids, such as fibrin, dead cells, etc. In the presence of food and oxygen this oxidation reaction can continue only so long as these products remain below a certain concentration. When this concentration is attained about the cells all activity ceases. For growth to take place in these cells a special mechanism for removing these products must be available, that is, it can take place only when the cells are brought into contact with certain colloidal materials having the property of absorbing these substances; and it continues until their concentration in these colloids reaches a certain concentration; then an equilibrium is established. Thus, we can see how the coagulable exudate in the wound forms the stimulus for growth and how growth ceases at the establishment of continuity of the part or how it fails through a failure of the formation of the exudate.

A careful study of the nail shows that it has a special mechanism for supplying colloidal materials and removing them continuously from the growing cells. The rhythmically contracting heart muscle cell has an electro-mechanical structure capable of splitting these substances into simpler compounds which are soluble in the circulating body fluids. The energy is transformed into work in these cells through the fact that the primary oxidation products decrease surface tension whereas their split products increase it.

Cancer cells have not been found to be different from actively growing normal cells. The study of them has, however, been so far limited.

SOME FACTORS REGULATING GROWTH.

By MONTROSE T. BURROWS.

(From the Department of Pathology, Johns Hopkins Hospital and University.)

(Abstract of article in The Anatomical Record, 1917, XI, No. 6.)

The problems under consideration in this paper are (1) the nature of the immediate conditions which lead to the failure of scar formation in many wounds or following many extensive inflammatory processes and (2) the general nature of the conditions which inhibit or allow the growth of connective tissue. It is well known that the most extensive inflammations of epithelial surfaces, as pneumonia, are most often followed by complete healing, while inflammations of the deeper connective areas are most frequently followed by the formation of a scar. In cancerous processes the connective tissue cells grow wildly at the expense of other parts.

Hertzler, a few years ago, came to the conclusion that the fibrinous exudate which forms in a wound, is the direct stimulus for the growth of the connective tissue cells. He noted that skin grafts take only when they become embedded in a layer of coagulable exudate. He also thought that the fibrin fibrils were transformed directly into the extracellular connective tissue fibrils. He had come to this last conclusion by means of a careful chronological study of intestinal adhesions and wounds induced by mechanical means in young rabbits of the same litter. He noted that previous to healing the fibrin is laid down in the form of fibrils. Connective tissue cells migrate among these fibrils. At a later period he found the fibrous tissue fibrils to occupy the same position and have the same arrangement as the fibrin fibrils. The wounds and adhesions had been removed at regular intervals, sectioned and stained. He was unable to see any evidence of the disappearance of fibrin, and the laying down of the connective tissue fibrils. Similar experiments were also made with wounds. In the summer of 1908, the author had the opportunity to study these experiments with Dr. Hertzler.

In the early studies of tissue culture made at Cornell University Medical College, it was noted that the fibrin fibrils in many of the cultures, after a considerable growth of connective tissue cells, stain the characteristic pink color, of white fibrous tissue with van Gieson stain. These observations were communicated to Dr. Hertzler, who reported them with his own studies ('13). Recently, Baitsell ('16), in Harrison's Laboratory, has made similar observations in tissue cultures. He did not observe the characteristic color reaction with the van Gieson stain.

Whether or not these pink-staining fibrils that had been observed in the tissue culture could be considered as true fibrous tissue, or merely structures simulating these fibers in their ability to absorb dyes, was a problem of interest. One of the objections to accepting them was the inconstancy of the appearance of pink-staining fibrils in many of the cultures.

In later studies of the growth of tissue *in vitro* several facts have been found, however, which would tend to substantiate this particular view. The first is that clot contraction or the formation of fibrin fibrils in the cultures of chicken tissue in plasma occurs only in the presence of connective tissue cells. Chicken plasma, when carefully prepared, free from previous tissue contamination, clots with the addition of a fragment of tissue to form a practically structureless jelly-like mass which has the same volume as the original fluid plasma. Any type of tissue conditions this primary clotting. In the presence of living connective tissue cells the clots later undergo contraction, while in the presence of epithelium they may undergo contraction but later liquefaction. Leucocytic or lymphocytic cells cause only slight liquefaction of these clots and very little, if any, contraction.

The second fact is that this contraction takes place only in the presence of living connective-tissue cells and then only after a considerable latent period. It fails entirely when the oxygen is replaced by nitrogen or hydrogen. It also fails when the tissue fragments have been heated for five minutes at 60° C.

In other words, it is evident that clot contraction is a phenomenon instituted by conditions quite different from those of primary clotting and it is a phenomenon which is brought about by the action of the products of metabolism of the connective tissue cells.

At another time the author studied more carefully the properties of the connective tissue cells. He has found that the cells of higher animals are not highly organized, but fluid-like systems. Their various manifestations of life such as movement, growth, etc., are differential surface tension phenomena under the control of a specifically organized environment. The food materials or energy producing substances in the cultures are not derived from the medium, but from the cells within the fragment. The growth that one observes in the cultures is none other than a simple transfer of materials from the cells of the center of the fragment or in a less favorable environment to those on the periphery or those which have been carried out into the medium through the interchange of substances between the fragment and the medium. This was shown by the fact that the cells can be grown in simple salt solution and, in the plasma cultures, growth ceases after a few transplants, the sum of the total growth being less than the original mass—or it represents what one might assume to be the original mass minus the energy of transfer. The cells that tend to break down in the fragment and lead to the greater growth of the connective tissue cells are not the connective-tissue cells but the epithelium, muscle cells, etc.

Again it was noticed that this growth takes place only in the presence of oxygen. It commences after a given latent period in the case of connective tissue, subsequently to the contraction of the clot. The cells grow actively for a time, gradually to come to rest. This reaction is one which apparently commences subsequently to the slow diffusion of substances between the fragment and the medium and proceeds until an equilibrium is established. In other words, it follows the curve of reaction of a heterogeneous physico-chemical system. The cells at the end of this reaction do not undergo, at least for a considerable time, any further change. They show no immediate disintegration. That this cessation of growth is not due to the exhaustion of oxygen or food materials is further shown by the failure of any change in the cells following the introduction of fresh air into the culture chamber, and by the fact that activity is again seen when the cells are transplanted to a new culture medium. On the other hand, that it is due to the accumulation of waste products is shown by the fact that the cells which tend to survive for the longer periods of time are invariably those cells which have grown out into the clot and have become completely surrounded by the contracted fibrin. It was of general interest in making these observations to note that this equilibrium which had been established in the tissue culture did not alone concern the cells which had migrated out and grown in the culture medium, but likewise those which remained within the fragment. With the cessation of growth of cells in the outer medium, disintegration with the liberation of energy-producing substances in the fragment also ceases. This is especially true when the fragments have

been placed in thick layers of plasma, so that they have become likewise completely surrounded by contracted clots. Many such cultures were kept for as long as six months at incubator temperature and in an ample supply of oxygen before any disintegration became apparent. Several were transplanted at this time and an active growth of cells was observed. The growth of the connective-tissue cell is apparently a tissue and not a cellular reaction. The failure of the connective-tissue cells to dissolve the fibrin and their ability to transform it into fibrils, leads to the belief that these fibrin fibrils form the superstructure upon which, or out of which, the connective-tissue fibrils are built. We observed pink-staining fibrils only in cultures of skin of foetal chickens. Whether the formation of the connective-tissue fibril is a body, rather than a connective-tissue cell reaction, is a question for solution.

It is well known that the growth of cells in the animal organism is not determined alone by food and oxygen but by other unknown conditions. The question naturally arises: Have these unknown conditions been found? Are the actual waste products of metabolism of these cells substances which are insoluble in body fluids; and is the cessation of growth of a part the result of the accumulation of these substances? One may assume that the fibrin fibrils are formed by the action of the products of metabolism of connective-tissue cells on the coagulable exudate, and that the cessation of growth in the wound is due to the accumulation of these substances in and about the growing cells. From these observations, one might readily define stimulation as any condition which would lead to the reduction of concentration in these substances. The stimulating action of fibrin is due to its ability to absorb these substances. To prove this more completely the author studied rhythmical activity in heart muscle cells as well as the growth of these and of connective-tissue cells in plasma cultures so arranged that the media could be continuously washed with a stream of serum. The rhythm of heart muscle fragment in simple hanging drop cultures is invariably intermittent. In the body it is a form of activity which continues throughout the life of the individual. In the cultures, where the medium was continuously washed by a stream of serum, the rhythm was not only greatly prolonged up to the time of complete exhaustion of the cells but it continued regular, while the growth of the cells was not changed but similar to that seen in the simple hanging-drop cultures. In a former paper before this society, the author presented facts to show that the contracting, embryonic heart-muscle cell has an organization which one might readily assume capable of splitting these insoluble waste products into simpler substances and of transforming the energy liberated with their formation into work of contraction.

Certain rapidly growing tissues, such as embryonal and rapidly growing tumors, grow readily in liquid media. This growth takes place only near the surface of the liquid. Cells suspended in liquid invariably round off and show no activity. The cells do not grow out into the liquid. It is of interest to note that adult tissues do not, however, grow readily in liquid media, whereas, on the other hand, they grow actively in plasma.

It was in the light of these facts and the more careful study of the properties of epithelia as well as leucocytic and lymphocytic cells that the general deductions as to the cause of the failure of scar formation in superficial inflammations of the epithelial surfaces were derived. Epithelial cells invariably bring about a rapid dissolution of the fibrin clots. When occurring in considerable numbers in a fragment of tissue, they invariably prevent entirely a growth of the connective-tissue cells. That the appearance of organization in the pneumonic lung probably indicates a complete destruction of the epithelium rather than the lack of leucocytes in the exudate was further suggested by the fact that the leucocytic infiltration in deep-seated inflammations is frequently as great as in the superficial ones. It is true that the leucocytes of man are richer in ferments than those of lower animals; the failure to observe any extensive liquefaction about the leucocytes of chickens would not indicate that this did not occur in human beings. On the other hand, it has been found that fragments of human connective tissue containing leucocytes grow readily in plasma clots when they are removed after 24 hours from the first culture to a drop of fresh plasma. This is not true of epithelium. The cells continue to liquefy the plasma even after many transplants, or until they are dead.

These observations are reported not only for the general bearing that they have on the nature of stimulation and the significance of extracellular substances in their relation to life processes, but also for their immediate significance for the better understanding of the actual conditions which regulate the growth of body cells. If these experiments are substantiated, showing, as it is believed they do, that growth is inhibited by the accumulation of insoluble waste products and permitted to proceed only by their removal, then the problem of the growth of the cell is brought into the domain of chemistry. Thus problems, such as those that confront us in cancer, are narrowed.

TRANSFUSION OF BLOOD BY THE CITRATE METHOD.

By V. P. W. SYDENSTRICKER, M. D., V. R. MASON, M. D., and T. M. RIVERS, M. D.

(Abstract of article in Jour. Am. Med. Ass., 1917, LXVIII, June 9.)

Transfusion of blood has been made simple by the use of anticoagulants, the citrate of soda having been shown to be the best and the least toxic. Two grams of sodium citrate given intravenously often cause chilly sensations and fever. However, in transfusion work two grams are practically never given at one time, as blood can be kept fluid by 0.25 per cent.

Donors should be carefully selected and all transmissible diseases excluded. A Wassermann test should be done on the donor's serum, if time permits. If cardiacs are used, a bacterial endocarditis should be excluded by blood culture if necessary. Malaria should be guarded against by the history and an examination of the blood.

After a healthy donor has been secured, agglutination tests should be properly carried out. This is done by mixing a drop each of the donor's serum and of the recipient's corpuscles suspended in physiological salt solution, and *vice versa*, and

incubating them for one hour at 37° C. Agglutination may take place quickly, but some severe reactions may be avoided if all tests are allowed to stand a full hour.

Human bloods fall into four groups, and group IV corpuscles (Moss) are not agglutinated by any other group's serum. Consequently group IV blood can be given to anybody without risk of a severe reaction. Nevertheless, it is better to centrifuge the citrated blood, pipette off the serum and make back to volume with physiological salt solution before giving.

The technic of citrate transfusion is very simple. The procedure can be carried out anywhere by one person if necessary, and the blood can be kept on ice for a number of hours without danger. The blood is drawn from the donor's median basilic vein by light suction into a graduated bottle, the citrate solution being mixed gradually by being run in through a graduated separating funnel. Ten cubic centimeters of 2.5 per cent sodium citrate solution will keep 90 c. c. of drawn blood from coagulating. After the blood has been drawn, it is transferred to an infusion bottle or salvasan apparatus and run into the recipient's median basilic vein.

Since the introduction of the citrate method into this hospital, 34 patients have received a total of 100 transfusions. The procedure has been carried out in a variety of conditions, as pernicious anæmia, secondary anæmia, burns, leukæmia, sepsis, typhoid fever and uræmia. The indications and results are similar to those that have been reported by other authors using the older methods.

Reactions after transfusions of all kinds are very interesting. Some are certainly due to carelessly performed agglutination tests, but others occur when the bloods match perfectly by the routine tests. As the question of reactions after repeated transfusions and often after the first transfusion of compatible blood is very interesting and little understood, the remainder of the abstract will be taken directly from the original paper:

The symptoms following transfusion of blood are in order of frequency malaise, slight elevation of temperature, chilly sensations, actual rigor, urticaria, pruritus, nausea, vomiting, lumbar pain, dyspnoea, cyanosis and hæmoglobinuria. Any single one or combination of these symptoms occurring within three hours after transfusion has been considered a reaction. Such symptoms have been present in 17 per cent of the cases reported. Most of the reactions were trivial, none was fatal. In every case the bloods were compatible by the routine tests.

The cause of these reactions is not definitely known. Typical anaphylactic-like reactions of mild grade are not uncommon and are quickly relieved by a hypodermatic injection of adrenalin. Three followed the transfusion of washed cells. One occurred in a patient with typhoid fever, following transfusion from a convalescent typhoid patient. Garbat has observed slight chills and some elevation of temperature following the intravenous injections of 2 grams of sodium citrate. In none of these cases has more than 1.75 grams of citrate been used. This quantity would hardly account for the symptoms. The reactions seem to bear no relation to the volume of the transfusion, many having followed small ones.

In this connection two cases of pernicious anæmia are of some interest. Mrs. J. B. received 9000 c. c. of blood by the Lindeman method between December 10, 1915, and February 14, 1916, without any severe reactions. During this admission her spleen was removed. She was readmitted in August, 1916, with extreme anæmia. Citrate transfusions from her husband and brother (each had been the donor several times previously) were followed by severe, almost fatal, reactions with hæmoglobinuria. A Lindeman transfusion, from a new donor, was followed by chill, high fever, coma and death. There were marked hæmoglobinuria and hæmoglobinemia. The case of H. A. P. is similar in many respects. Splenectomy and repeated transfusions had been performed during previous admissions. Following a citrate transfusion from a previous donor he had a severe reaction, chill, stupor and hæmoglobinuria. A new donor was secured, but a similar reaction followed. No more transfusions were attempted.

These two cases have suggested the possibility of the formation, after repeated transfusions, of antibodies to homologous blood which are not demonstrable *in vitro*. In both after the occurrence of severe reactions, tests were done with particular care. Gross and microscopic preparations were made with varying dilutions of the donor's and recipient's sera. These were incubated one hour at 37° C., then put on ice for 24 hours and again incubated. There was no agglutination or hemolysis. Similar tests were done in the choosing of subsequent donors with negative results, yet transfusion from these donors gave most severe reactions. Without attempting to explain these, it would seem that transfusion is a self-limited method of treatment in pernicious anæmia, since after a certain number of transfusions homologous blood may cause reactions of increasing severity. We have been unable to produce any similar result experimentally in normal animals.

SURFACE STERILIZATION OF TISSUE FOR BACTERIAL STUDIES.

By D. M. DAVIS, M. D., and ROBERT ROSEN.

(From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Md.)

(Abstract. To appear in full in the Journal of Infectious Diseases shortly.)

In a series of experiments for the purpose of studying the bacterial content of the prostate, certain difficulties were encountered with the methods commonly described for making cultures from tissues. It was found that by using the method recommended by Rosenow certain discrepancies occurred in the results which suggested that they may have been due to contamination introduced at some point between the time the tissue was exposed by the surgical scalpel and the final closure of the culture tube. In order to decide this question decisively it was determined to put a close check on each step in this process.

Grinding up glandular tissues in a sterile mortar, flaming the tissues, dipping them in boiling saline, water or hot oil, were methods used by previous investigators. The time element varies with the size of the tissues used. Owing to the

fact that the air-chamber recommended by Rosenow, as found on the market, is not air-tight, that it is very unstable, that only one hand can be introduced and that the large cotton plug used is difficult to manage, it was decided to design a new chamber to eliminate these difficulties. The chamber, as finally constructed, is made of heavy tin with large panes of plate glass at both the top and front, a handhold at each end, to which canvas gloves are attached, so that both hands can work on the inside of the box, and an opening on the metal side for introducing the necessary materials and tissue. The flange of this opening is one-fourth inch smaller than the cap, so that the edge of the cap never comes in contact with the flange. This eliminates the cotton plug.

The apparatus was tested out for its sterility by placing in it tissue which had been autoclaved, its surface later inoculated with *Staphylococcus aureus* and again sterilized by the methods to be described. The hands were rendered relatively sterile and non-bactericidal, inoculated with *B. violaceus*, inserted into the canvas gloves attached to the chamber and the tissue was cut up and ground for 30 minutes, poured into a test tube and removed from the chamber, and plated, 1 c. c. per plate being used. In this process the sterile broth and the tissue were the only articles introduced into the chamber after the chamber had been sterilized. In 12 such experiments the plates remained sterile.

Having eliminated the dangers of contamination from the chamber the methods of surface sterilization of tissues to be used in bacterial study had to be checked up. For this autoclaved tissue was inoculated superficially or deeply with *Staphylococcus aureus*.

OUTLINE OF METHOD.

1. Mortars or evaporating dishes and pestles, scissors and tissue forceps are placed in a wire basket and sterilized in the hot-air oven for one hour at 190° C., the mortars or dishes being upside down.

2. Autoclaved kidney or liver is placed in a sterile glass jar containing tissue forceps and scissors, and cut into pieces about 1.5 x 2 x 1.5 cm. in size.

3. A piece of tissue is immersed in an emulsion of a 24-hour broth culture of the organism for an instant.

4. The tissue is placed in hot liquid paraffin, boiling saline or passed through a bunsen flame for the desired length of time.

5. It is removed to a sterile mortar, in which are 10 c. c. of sterile bouillon, and ground with the sterile pestle.

6. One cubic centimeter of this tissue emulsion is removed and plated. The procedure is repeated, the time of heating and media being changed as desired.

7. As a check on the tissue used, a piece which has not been inoculated is emulsified and 1 c. c. of this emulsion is plated.

8. As a check on the organism and to have a culture where no sterilizing methods have been used with which to compare the growth from the heated tissue, a piece of tissue is dipped in a bacterial emulsion and run through just as is done to the pieces which have been heated.

9. For deep tissue inoculation a hypodermic syringe is used, the bacterial emulsion being forced into the interior of the tissue and the whole then dipped in the same emulsion. The procedure from this point is the same as above. In this way the amount of heat necessary to destroy the surface bacteria without interfering with the organisms that are on the interior could be determined.*

DISCUSSION.

1. The time required for surface sterilization by the boiling salt solution was found to be 25 seconds, which is sufficient to sterilize the tissue throughout, giving no margin of safety.

2. The same was true for the sterilization by the bunsen flame method, the required 25 seconds being sufficient to char the tissue.*

3. For liquid paraffin, at 180° C., the thermal death point was below 10 seconds for surface sterilization. This is not sufficient to destroy bacteria on the interior which requires 20 seconds. Ten seconds seemed to be sufficient for surface sterilization, leaving a wide margin of safety. In the case of a thermosensitive organism the time and temperature factors might have to be varied.

SUMMARY.

1. With the air chamber and technique described in this paper, danger of contamination from the outside during the making of cultures from tissues is reduced to the minimum.

2. It is apparent that the boiling water method as formerly used is inadequate for surface sterilization, and that the time required to sterilize the surface with certainty approaches that sufficient to sterilize the gland completely.

3. The same objections apply to the bunsen flame; the flame either does not reach every part of the tissue or the charred tissue acts as a non-conductor of heat.

4. The hot oil method of sterilization answers the purpose better than the preceding two methods, inasmuch as at a temperature of 180° C., surface bacteria will be destroyed in 10 seconds without any apparent interference with the organisms in the interior of the tissue, which are not killed unless it is heated for 20 seconds.

5. In view of the stress laid on the bacteriology of glandular tissues in relation to the etiology of disease, it becomes apparent at once that surface sterilization is of the utmost importance. Having obtained a satisfactory method of surface sterilization, more confidence can be placed in the results obtained in future studies.

* It is understood that this is an exaggeration of the infection usually present on tissues to be cultured, but that such infection is not negligible is shown by a recent culture of 10 c. c. of broth into which a piece of prostate, dropped by the operator into a sterile glass jar, had been placed for a moment. A plate made with 1 c. c. contained 250 colonies. In another case, 1 c. c. of broth in which the prostate had been immersed produced 250 colonies, whereas after immediate surface sterilization for eight seconds in liquid paraffin at 180° C., emulsifying the tissue in which a pus cavity was found and plating 1 c. c. of this emulsion, the colonies were innumerable.

NOTES ON NEW BOOKS.

The Kinetic Drive. By GEORGE W. CRILE, M. D. Wesley M. Carpenter Lecture, 1915. Illustrated. 8 vo. 71 pages. Cloth, \$2.00. (Philadelphia and London: W. B. Saunders Company, 1916.)

Man—An Adaptive Mechanism. By GEORGE W. CRILE, M. D. 8 vo. 387 pages. Cloth, \$2.50. (New York: The Macmillan Company, 1916.)

The second of these books gives a fuller presentation of essentially the same topic of which the first book treats in a more summary and more pointed manner. The documentary material is to appear in a full account of the researches from which the illustrative material has been drawn. Strictly speaking, both works represent the formulation of the personal philosophy of one of our foremost surgeons. It is an emphatic appreciation of the functional-mechanistic view of man in action, a view of life as a drive, a struggle, a battle, with an interest in the rôle of physics and chemistry as keen and unrelenting as the interest in heredity and selection shown in Darwin and his followers. We might speak of a revival of Darwinian philosophy with emphasis on the conquests of modern physiology. In all the facts of anatomy and physiology—"in the complete life cycle of the individual from conception to death we see clearly here and dimly there the mechanisms by means of which a sensitive being immersed in a hostile environment effects survival—we see man—an adaptive mechanism." War and struggle seem to dominate. "In understanding the physical basis of the action of faith and hope, as opposed to fear, despair, anger and grief, we have at our command a concrete force which can be efficiently used to protect the individual. As the knowledge of disgrace and punishment prevents dishonesty; as the knowledge of contagion prevents exposure to contagion, so the mere knowledge—the conviction—that excessive anger, work, jealousy, envy, worry or grief cause physical damage as serious as that produced by infections or crushing blows will constitute a powerful protection to man. The knowledge that these activations not only decrease the power of the individual to do his work, but ultimately cause numerous diseases as well, will result automatically in arousing the instinct of self-preservation, which will surround the individual with a protecting circle, through which anger, jealousy, grief, and worry cannot penetrate, just as the zone of local anesthesia in the anociated surgical operation is an impenetrable barrier between the brain and the knife, making the surgical operation shockless."

The striking feature of this intensely dynamic conception is Crile's willingness to give prominent attention to the emotions. The author's interest in surgical shock and the obviously intense interest in Darwinian philosophy and, we may infer, a keen feeling against non-biological conceptions, have led him to the formulation of a Kinetic System, with the brain as the initiator and driver, the adrenals as the "oxidizers, making possible the transformation of energy and the neutralization of the resulting acid products," the liver as fabricator and storehouse of fuel, the muscles the transformers of energy into heat or motion, the thyroid the organ of speed control through facilitation of the passage of ions. With this goes the interest in a uniform explanation of "acute activation of the organism by infection, by foreign proteins, by exertion, by emotion, and by physical injury." "As our evidence has accumulated, we have come to see that more of the chronic diseases result from the *excessive work thrown upon certain organs for the elimination of the superabundant acid products of energy transformation than result primarily from the energy transformation itself*" (p. 10). "The kinetic drive harmonizes many facts in the great clinic of life as well as in the restricted clinics of medicine; it emphasizes the value of a mechanistic view of life in the study of both normal and pathologic processes; and

it suggests a philosophy of life by means of which self-preservation may be secured through kinetic control." This control can be attained by guarding against overstimulating factors, by the substitution of hope for fear, by narcotics, and possibly even by the reducing in size of the activating organs, the adrenals and thyroid—by a "dekinetizing" operation.

There is hardly a doubt that a strongly individual positive revulsion against anti-mechanistic and non-dynamic views of life and attitudes in medicine finds its expression in these books. They deal with the push and drive of life and urge upon the physician to heed the importance of emotion as well as of other factors in life, and to make the assimilation acceptable, the mechanistic presentation of the many factors to be considered is sought as the general solution.

The work is very personal. There is little effort to assimilate the material and discussions of other investigators and thinkers or to point out the author's relation to other viewpoints. The foundation for the claims are largely furnished by the physiological and histological researches of Crile's clinic and laboratory. The one difficulty for other workers in dealing with Crile's facts lies in Crile's tendency to argue from extreme results and observations which might be open to more than one interpretation and would not necessarily form a sound foundation for the rank and file of experience. The histological pictures of the cerebellum in my own series of unselected but well controlled observation tend to convince me that they do not form as striking an index of the status of the whole organism as Crile's account might suggest. The extension of the study to less extreme degrees of change will make it clear that other *functional* methods cannot be dispensed with. And with this broadening out, it may well be that there will be space for less extreme mechanistic conceptions for a physician's philosophy.

The great value of the two books lies in the vigorous effort at functional formulation of human problems. They present a forceful plea for a reanimation of medical science. Science has to sum up its facts and outlooks occasionally. Even if Crile's claims in detail should not stand and the extreme cautions of "anociated surgical operation" might not be so strictly called for, Crile has succeeded in reintroducing some consideration for emotions, and he is paving the way for a wider interest in Cannon's work and other modern contributions. That one has a feeling of too much being promised in a simple scheme, and that through such simple solutions the patience with the really needed more complicated types of work and conceptions might suffer, need not detract from Crile's service to medical thoughtfulness. Some workers are driven by enthusiasm, others more by a stubborn critical determination. The mutual and frank discussion of the two types will bring us further than extreme perfectionism and conservatism.

Surgery in War. By ALFRED J. HULL, F. R. C. S., Major, Royal Army Medical Corps; with a Preface by SIR ALFRED KEOGH, K. C. B., M. D., Director-General Army Medical Service. Cloth, \$4.00. Pp. 390, with 81 illustrations. (Philadelphia: P. Blakiston's Son & Co., 1916.)

The present war has given surgeons and sanitarians wonderful opportunities for observation. This little book is a compilation by Major Hull of several articles on various phases of war surgery. The authors are all members of the British Medical Corps and men of renown. The arrangement is logical and the discussions are, on the whole, clear and complete. There is, however, some tendency to repetition, particularly in the matter of the new irrigation treatment of wounds.

The book would be of much more scientific value if it contained statistics. The author apologizes for this defect and lays the blame on the censor.

H. R. S.

BOOKS RECEIVED.

- The Medical Clinics of Chicago.* Vol. II, No. 2, September, 1916. 8°. 417 pages. W. B. Saunders Company, Philadelphia and London.
- Studies in Blood Pressure, Physiological and Clinical.* By George Oliver, M. D., Lond., F. R. C. P. Edited by W. D. Halliburton, M. D., F. R. S. Third edition. 1916. 8°. 240 pages. Paul B. Hoeber, New York.
- Practical Bacteriology, Blood Work and Animal Parasitology, Including Bacteriological Keys, Zoological Tables and Explanatory Clinical Notes.* By E. R. Stitt, A. B., Ph. G., M. D. Fourth edition, revised and enlarged. 1916. 12°. 497 pages. P. Blakiston's Son & Co., Philadelphia.
- Burdett's Hospitals and Charities, 1916.* Being the Year Book of Philanthropy and the Hospital Annual. By Sir Henry Burdett, K. C. B., K. C. V. O. Twenty-seventh year. 1916. 12°. 1070 pages. The Scientific Press, Limited, London.
- American Proctologic Society.* Transactions of the Eighteenth Annual Meeting. 1916. 8°. 144 pages. Printed by The Proctologist, St. Louis, Mo.
- Applied Immunology.* The Practical Application of Sera and Bacterins Prophylactically, Diagnostically and Therapeutically; with an Appendix on Serum Treatment of Hemorrhage, Organotherapy and Chemotherapy. By B. A. Thomas, A. M., M. D., and R. H. Ivy, M. D., D. D. S. Five colored inserts and 68 illustrations in the text. Second edition revised. 1916. 8°. 364 pages. J. B. Lippincott Company, Philadelphia and London.
- Pharmacology and Therapeutics.* For Students and Practitioners of Medicine. By Horatio C. Wood, Jr., M. D. Second edition. 1916. 8°. 455 pages. J. B. Lippincott Company, Philadelphia and London.
- A Text-Book of Practical Therapeutics,* with Especial Reference to the Application of Remedial Measures to Disease and their Employment upon a Rational Basis. By Hobart Amory Hare, M. D., B. Sc. Sixteenth edition, enlarged, thoroughly revised, and largely rewritten. Illustrated with 149 engravings and seven plates. 1916. 8°. 1009 pages. Lea & Febiger, Philadelphia and New York.
- Three Contributions to the Theory of Sex.* By Prof. Dr. Sigmund Freud, LL. D. Authorized Translation by A. A. Brill, Ph. B., M. D. With Introduction by James J. Putnam, M. D. Second revised and enlarged edition. Nervous and Mental Disease Monograph Series No. 7. 1916. 8°. 117 pages. Nervous and Mental Disease Publishing Company, New York.
- The Significance of Psychoanalysis for the Mental Sciences.* By Dr. Otto Rank and Dr. Hanns Sachs. Authorized English translation by Dr. Charles R. Payne. Nervous and Mental Disease Monograph Series No. 23. 1916. 8°. 127 pages. Nervous and Mental Disease Publishing Company, New York.
- Manual of Chemistry.* A Guide to Lectures and Laboratory Work for Beginners in Chemistry. A Text-Book Specially Adapted for Students of Medicine, Pharmacy and Dentistry. By W. Simon, Ph. D., M. D. and Daniel Base, Ph. D. Eleventh edition, thoroughly revised. With 55 illustrations, one colored spectra plate and six colored plates representing 48 chemical reactions. 1916. 8°. 648 pages. Lea & Febiger, Philadelphia and New York.
- Mechanisms of Character Formation.* An Introduction to Psychoanalysis. By William A. White, M. D. 1916. 8°. 342 pages. The Macmillan Company, New York.
- Royal College of Surgeons of England.* Calendar, August 1, 1916. 8°. 407 pages. Taylor & Francis, Red Lion Court, Fleet Street, London.
- Syphilis.* By Loyd Thompson, Ph. B., M. D. Illustrated with 77 engravings and seven plates. 1916. 8°. 515 pages. Lea & Febiger, Philadelphia and New York.
- Blood Pressure, from the Clinical Standpoint.* By Francis Ashley Faught, M. D. Second edition, thoroughly revised. 1916. 8°. 478 pages. W. B. Saunders Company, Philadelphia and London.
- Constipation, Obstipation and Intestinal Stasis (Auto-Intoxication).* By Samuel Goodwin Gant, M. D., LL. D. Second edition, enlarged with 259 illustrations. 1916. 8°. 584 pages. W. B. Saunders Company, Philadelphia and London.
- University of Sydney.* Calendar of the University of Sydney for the Year 1916. 8°. 695 pages. Angus & Robertson, Ltd., Sydney.
- Royal Academy of Medicine in Ireland.* Transactions. Vol. XXXIII, 1915, 465 pages and Vol. XXXIV, 1916. 288 pages. Edited by J. Alfred Scott, M. A., M. D., F. R. C. S. I. 8°. John Falconer, Dublin; Baillière, Tindall & Cox, London; James Thin, Edinburgh; John Wright & Co., Bristol.
- United States. Department of Commerce. Bureau of the Census.* Sam. L. Rogers, Director. Mortality Statistics, 1914. Fifteenth Annual Report. 1916. 4°. 714 pages. Government Printing Office, Washington.
- United States. Department of Commerce. Bureau of the Census.* Sam. L. Rogers, Director. Financial Statistics of States, 1915. 1916. 4°. 125 pages. Government Printing Office, Washington.
- Studies from the Rockefeller Institute for Medical Research.* Reprints. Volume XXV. 1916. 8°. 583 pages. The Rockefeller Institute for Medical Research, New York.
- The National Association for the Study and Prevention of Tuberculosis.* Transactions of the Twelfth Annual Meeting. 1916. 8°. 517 pages. The National Association for the Study and Prevention of Tuberculosis, New York.
- A Text-Book of Organic Chemistry.* For Students of Medicine and Biology. By E. V. McCollum, Ph. D. 1916. 16°. 426 pages. The Macmillan Company, New York.
- Materia Medica for Nurses.* By A. S. Blumgarten, M. D. Second edition, completely revised, with additions and new illustrations. 1916. 8°. 651 pages. The Macmillan Company, New York.
- The Pathology and Differential Diagnosis of Infectious Diseases of Animals.* Prepared for Students and Practitioners of Veterinary Medicine. By Veranus Alva Moore, B. S., M. D., V. M. D. Fourth edition revised and enlarged with 120 illustrations. 1916. 8°. 593 pages. The Macmillan Company, New York.
- Report of the First Expedition to South America, 1913.* Members of the Expedition Richard P. Strong, Ernest E. Tyzzer, Charles T. Brues, A. W. Sellards, J. C. Gastiaburu. Harvard School of Tropical Medicine. 1915. 4°. 220 pages. Harvard University Press, Cambridge.
- United States. Navy Department. Bureau of Medicine and Surgery.* Annual Report of the Surgeon General, U. S. Navy, to the Secretary of the Navy. For the Fiscal Year 1916. 8°. 104 pages. Government Printing Office, Washington.

United States. Public Health Service. Annual Report of the Surgeon General of the Public Health Service of the United States. For the Fiscal Year 1916. 8°. 421 pages. Government Printing Office, Washington.

American Surgical Association. Transactions. Volume XXXIV. Edited by John F. Binnie, M.D. 1916. 8°. 540 pages. William J. Dornan, Philadelphia.

Teacher's Guide for Blumgarten's Materia Medica for Nurses. By A. S. Blumgarten, M.D. 1916. 8°. 16 pages. The Macmillan Company, New York.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. By leading members of the medical profession throughout the world. Edited by H. R. M. Landis, M.D. Volume IV. Twenty-sixth series. 1916. 8°. 307 pages. J. B. Lippincott Company, Philadelphia and London.

Notes on the Causation of Cancer. By the Hon. Rollo Russell, with a Preface by Dr. Dawtrey Drewitt. 1916. 12°. 116 pages. Longmans, Green & Co., London.

The Rockefeller Foundation. Annual Report, 1915. [1916.] 8°. 377 pages. Published by the Rockefeller Foundation, 61 Broadway, New York.

Cardio-Vascular Diseases. Recent Advances in their Anatomy, Physiology, Pathology, Diagnosis and Treatment. By Thomas E. Satterthwaite, A.B., M.D., LL.D., Sc.D. 1913. 8°. 166 pages. Lemcke and Buechner, New York City.

Bellevue and Allied Hospitals. City of New York. Fourteenth Annual Report, January 1, 1915 to December 31, 1915. 8°. 157 pages. New York City.

My Birth, the Autobiography of an Unborn Infant. By Armenouhie T. Lamson. 1916. 12°. 140 pages. The Macmillan Company, New York.

Public Health Nursing. By Mary Sewall Gardner, R. N. With an Introduction by M. Adelaide Nutting. 1916. 12°. 372 pages. The Macmillan Company, New York.

The Animal Parasites of Man. By H. B. Fantham, M. A. Cantab., D. Sc., Lond., J. W. W. Stephens, M. D. Cantab., D. P. H. and F. V. Theobald, M. A. Cantab., F. E. S., Hon. F. R. H. S. Partly adapted from Dr. Max Braun's "Die Tierischen Parasiten des Menschen" (4th Edition, 1908), and an Appendix by Dr. Otto Seifert. 1916. 8°. 900 pages. William Wood & Co., New York.

American Gynecological Society. Transactions. Volume XLI, for the year 1916. 8°. 726 pages. William J. Dornan, Philadelphia.

Cornell University Medical Bulletin. Volume VI, Number 2, October, 1916. Studies from the Department of Medicine including Applied Pharmacology and Dermatology. 8°. 355 pages. Published by Cornell University, New York City.

Interstate Commerce Commission. Thirtieth Annual Report. 1916. 8°. 248 pages. Government Printing Office, Washington.

AN APPEAL TO THE MEDICAL PROFESSION OF THE UNITED STATES.

The Surgeon General's Office has appealed to the medical press of this country for aid in securing the quota of physicians necessary for the care of the great army now in course of organization.

The Medical Departments of the Government are responsible for the examination of the recruits, the hygiene of camps and the care of the sick and wounded. The Surgeons General have not as yet been given full authority and the means to meet this responsibility.

The President and Congress can give the Surgeons General full authority and ample means, but except by the draft neither the President nor Congress is able to give them a sufficient number of men from the medical profession, as it is a volunteer service. Consequently, if the Medical Departments are furnished with the authority and the means, they will still be unable to do their work unless the medical profession of the country, and particularly the younger men, respond more freely than they have done up to this time.

In the army hospitals and first aid work abroad, in the vast concentration camps so soon to be organized in this country, and in every branch of the naval service there is an urgent demand for each physician who can and will offer his services. In the work our country has pledged itself to do, the need for doctors is imperative. Estimates give the figure of 20,000

physicians as the minimum number necessary for this work. Only about 6000 are at present enrolled. These figures speak for themselves.

Commissions in the Medical Reserve Corps are accorded on the basis of First Lieutenant, Captain and Major, with respective salaries of \$2000, \$2400 and \$3000 a year. Applicants may apply directly to the various examining boards throughout the different states and complete all preliminary arrangements without reference to the Surgeon General's Office. The completed papers should be forwarded directly to the Surgeon General by the president of the examining board. A complete set of papers must contain the physical examination, report of the examiner as to mental, moral and physical qualifications, a personal history form filled out by the applicant and sworn to before a notary, and a certificate of state registration (except where this year's graduates have not had time to take their State Board examination). Two letters should also be sent certifying as to citizenship and moral qualifications, and if of alien birth, a certificate of naturalization.

Further information may be obtained from the State and County Committees of National Defense, or directly from Surgeon General W. C. Gorgas, of the Army, or Surgeon General W. C. Braisted, of the Navy, Washington, D. C.

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UNIVERSITY OF KENTUCKY
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EMBRYOMAS IN PLANTS. (PRODUCED BY BACTERIAL INOCULATIONS.)

By ERWIN F. SMITH.

(From the Laboratory of Plant Pathology, Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C.)

In April, 1916, I announced the discovery of a new type of crown gall, *i. e.*, one containing numerous leafy shoots, and showed that I could produce it at will by making my bacterial inoculations in leaf axils where there is a dormant bud; that exceptionally in tobacco I had produced it on the blade of the leaf where there were no buds, also once in an internode; that frequently the secondary tumors were of the same type as the primary tumor, *i. e.*, full of perishable leafy shoots; and, finally, that I regarded it as a true embryoma comparable to those occurring in animals.¹ Since then I have been experimenting continuously and now wish to offer further data on the production of these anomalous crown galls which, following Adami's terminology of tumors (Principles of Pathology), I consider to be atypical teratoid tumors.² With one exception (Fig. 63), all the photographs and photomicrographs I shall use for illustration are of tumors which are the result of pure-culture bacterial inoculations, although I have since discovered that leafy crown galls occur in nature on various plants, *e. g.*, on the rose and on the carnation.

Atypical (that is, embryonal) teratoid tumors have now been produced by the writer in plants of the following genera: Pelargonium, Nicotiana (2 sp.), Lycopersicum, Citrus, Rici-

nus, Impatiens, Hibiscus, Allemanda, Mangifera, Opuntia, Fuchsia, Tropæolum, Coleus, Beta, Rosa, and Brassica (both cabbage and cauliflower), using pure cultures of the hop strain of the crown-gall organism (*Bacterium tumefaciens*), introduced by needle-pricks. These genera belong to 15 different families of plants. The writer has also produced them on the carnation (*Dianthus*) with a strain of the crown-gall organism cultivated from a leafy tumor on *Dianthus caryophyllus*, and on a third species of tobacco (*Nicotiana langsdorfi*) with a strain of the crown-gall organism (Resistant Daisy) cultivated from a tumor on the Paris daisy (*Chrysanthemum frutescens*). From this it is reasonable to suppose that embryonal teratoid tumors can be produced in a great variety of plants and as readily as the ordinary crown galls. All that is necessary is to introduce the crown-gall bacteria into the growing tissues of susceptible species in the vicinity of totipotent cells. These totipotent cells may be either dormant axillary buds or meristematic cells remote from leaf axils and buds, or bud anlage. These cells have the potentiality of germ cells whatever their origin, *i. e.*, somatic or germinal. It was to the production of embryomas on leaves and on stem internodes from ordinary meristem cells, presumably somatic cells, that a part of my energies were directed during the summer of 1916.

This paper treats principally of crown-gall teratoids produced on Nicotiana and Pelargonium, but photographs of a few other plants are introduced for specific purposes, *e. g.*, of

¹ The Journal of Cancer Research, April, 1916.

² This paper is an expansion of the latter part of an address given by permission of the Secretary of Agriculture before The Johns Hopkins Medical Society, December 18, 1916, entitled: "Is there any real relation between crown gall of plants and cancer?"

the common garden balsam and of *Tropæolum* to show at the top of the plant tumors covered with roots, of *Ricinus* and daisy to show tumor strands, of rose to show return of tumors after destruction, of okra to show encysted tumors becoming malignant, and of sunflower to show invasion of normal tissue by the stroma and other elements of the tumor. It deals chiefly with the result of efforts: (1) To produce these peculiar hyperplasias in the middle of internodes remote from axillary buds and where no shoots ordinarily develop;³ (2) to determine under what conditions the tumors can be made to grow as ordinary sarcomata destitute of teratoid elements, or can be made to produce (a) roots, (b) leafy shoots, (c) floral abortions, or (d) a mixture of all of these teratoid elements; (3) to determine what particular tissues of the young internode (cortex, cambium, pith, etc.) may give rise to the teratoids, and what can produce only sarcomata; (4) to record the inception and progress of these tumors by means of good photographs, so as to bring before the reader clearly their astonishing proliferation and equally rapid decay; (5) to demonstrate by photomicrographs made from stained serial sections the embryonic and fragmentary nature of the teratoid elements occurring in the depths of these tumors; and (6) the existence of jumbled sarcomatous elements in their vicinity.

Incidentally some interesting records have been obtained on fasciation and various related abnormalities (flattening and fusion of organs or imperfect development of parts), on variability in rate of tumor growth, on secondary infections, and on failure of tumors once started to continue to grow. The last experiment on tobacco (September 7, 1916) also shows the germicidal effect of collodion used to cover the wounded surface immediately after the bacterial inoculation. The photographs speak for themselves and only a modicum of text is necessary.

EXPERIMENTS ON TOBACCO.

A. IN THE HOthouse.

The plants used for these experiments exclusive of some broad-leaved, tall, ornamental, white-flowered tobaccoes (*Nicotiana glauca*), which also yielded teratoids but which will not be referred to again here, were hybrid (Connecticut-grown Havana seed) hothouse specimens of the Sumatran wrapper leaf type of *Nicotiana tabacum*. Some were grown in large pots; others had rooted through the bottom of smaller pots into a central bed. All of the inoculations here described, except those on the plant first figured (Fig. 1), which were in part at least into the leaf axils, were made on the main axis of the plant in the middle of internodes, i. e., remote from buds. For the non-botanical reader it may be said that the stem or main axis consists of *nodes* and *internodes*. The leaves arise at the nodes, wherein there is a great interweaving and anastomosing of vessels, and in each leaf axil there is a dormant bud capable of growing into a shoot if conditions are favorable.

These buds presumably furnish the teratoid elements of axillary tumors such as those already described (*l. c.*, Figs. 66 and 76) and those shown in Fig. 1 of this paper. In the internodes, on the contrary, the vessels run parallel to each other and to the longer axis of the stem in sheathing organs known as the wood cylinder (xylem) and as the inner bark cylinder (phloem). The bark cylinder is surrounded by a conjunctive tissue called *cortex*, and the inner (wood) cylinder is filled with a conjunctive tissue called *pith*. The two cylinders (of wood and of bark) are separated by a third thin cylinder of meristem known as *cambium*. This triple cylinder (phloem, cambium, and wood) is not a unit but a complex composed of many distinct groups of vessels known as vascular bundles. The vascular bundles in young stems radiate from the pith to the cortex like spokes from the hub of a wheel (see text figure), and each, therefore, includes its own portion of inner phloem (wanting in many species) protoxylem, xylem, cambium, phloem, and protophloem. Standing in the cortex, usually next to the phloem, are also in many plants bundles of strengthening fibers known as hard bast or bast fibers. These vascular bundles are separated radially by thin wedges of conjunctive tissue known as medullary rays, which in young stems begin in the pith and end in the cortex and which are added to tangentially from either side of the medial (cambium) line just as are the vascular bundles. In stems more than a year old new wedges of conjunctive tissue, secondary medullary rays, are intercalated from the cambium, and these, of course, do not reach to the pith. In very young stems the cortex is covered by a delicate living membrane (the epidermis); in older stems the epidermis is replaced by a many-layered, impervious, tough membrane (cork). As stems grow, numerous cork cambiums are formed cutting out peripheral portions of the stems and forming dead protective layers, often of considerable thickness (the outer bark). In some plants, *e. g.*, tobacco, which are then said to have bi-collateral bundles, there are two phloems, i. e., in addition to the ordinary phloem outside the cambium there is an inner phloem lying between the pith and the wood (see text figure, p. 288).

The internodes selected for the experiments were severed about midway of the nodes at right angles to the longer axis of the stem by means of a sharp razor and crown-gall bacteria from young agar-streak cultures (many removes from the original colony) were pricked into the cut surface (not injected) by means of a delicate steel needle. The needle-pricks varied in depth from 1 to 3 mm. The organism used for all of the experiments detailed in this paper was the hop strain of *Bacterium tumefaciens* isolated in January, 1908, and cultivated in my laboratory on various media for eight years without inoculation (this particular line of the descent), then inoculated by the writer into sunflower (in 1915) with the production of tumors, from one of which it was re-isolated by means of an agar-poured plate and subcultured from a single colony called "Sunflower Colony 1." In all cases the inoculations were made from young agar-streak cultures two to six days old.

³ See the *Journal of Cancer Research*, Vol. I, April, 1916, Plate XIX, Fig. 71, and context, where the first internodal tumor of this type is figured and described.

Done out-of-door on large, but slow-growing plants (Fig. 49), exposed to the hot sun, to dry air and to insect depredations, these experiments failed almost completely (in 21 out of 51 shoots, entirely), but in the clean, moist hothouse failures on soft, well-nourished plants were exceptional, *but were not exceptional on slow-growing firm ones.*

Fig. 2 illustrates the type of stem selected for inoculation (at X). Fig. 3 shows the appearance of one of the checks at the end of four weeks when a new top has developed from an axillary bud below at the left of the main axis, which meanwhile has trebled in diameter. No growth has taken place from the cut surface, and no growth ever does take place from such cut surfaces, as everyone knows who has ever had to do with the cultivation and pruning of tobacco.* When, however, such internodal cut surfaces are inoculated with pure cultures of *Bacterium tumefaciens* S. and T., they develop tumors of two sorts in varying numbers and with variable degrees of rapidity, the kind of tumor depending on the particular tissues stimulated. One type in my judgment is a plain sarcoma (the ordinary crown gall); the other is a sarcoma filled with proliferating teratoid elements especially with abortive leafy shoots, frequently to the number of several hundred.

*But the tendency is always there, if the stimulus is strong enough, not only in tobacco but probably in all other plants, and presumably also in all animals, since a great many plants and animals are known to give rise readily to adventive buds even under a slight stimulus, *e. g.*, willows and begonias; hydras and tubularias. Just what the stimulus is in many cases remains to be worked out. The shoots are especially apt to appear when the plant or animal has been wounded or otherwise thrown out of balance. Such shoots are normal, or pathological only to the extent of being more or less fused, crowded, distorted and starved. For these reasons some of them should undoubtedly be classed as typical (non-cancerous) teratoids. Several interesting cases in plants have come to the writer's attention lately and will be described elsewhere. These are on tomato, cauliflower, cabbage, pond lily, etc. In one very curious variety of begonia (*Begonia phillomaniaca*) buds in great numbers grow out of many parts of the leaf and stem on the slightest provocation (*vide* figures in Bailey's "Cyclopedia of American Horticulture," 1st ed., Vol. I, p. 146, and observations by Bateson in his "Problems of Genetics," pp. 50-51, where the species is considered to be a hybrid). In a begonia of this variety now growing in one of our houses, on an upper branch of the main axis (which was cut away), a single lower leaf has developed more than 600 of these diminutive shoots (embryo plants), but the remaining leaves on this shoot have developed only a few, the average number per leaf being 23. On this plant, their number is roughly proportional to the age of the organ bearing them, that is, proceeding from the lowermost leaf to the uppermost one the numbers of adventive shoots are 616, 56, 35, 0, 0. The same law holds good for the shoot axis bearing these leaves. It is 6 inches long and the adventive shoots from its surface are: Lower 2 inches, 56 (nearly all from lower half); middle 2 inches, 15; upper 2 inches, 2. But I have other plants the middle leaves of which bare most shoots. These are cuttings of last winter. Possibly loss of water due to the cutting may have caused this excessive germination of totipotent cells in particular leaves. All the leaves might lose water equally, or even the older ones most, and yet only the younger ones (topmost at time of cutting) be in condition to send out great numbers of shoots, *i. e.*, sufficiently meristematic to respond freely to the stimulus (see Mechanism of Tumor Growth, *l. c.*).

My first series of hothouse inoculations using the cut surface of tobacco internodes was made on May 31, 1916; my second on July 7; my third on July 29; my fourth on August 1; my fifth on September 7. The following is a brief account of these experiments, all internodal be it understood:

I. *Inoculations of May 31.*—All but one of the 12 inoculations of May 31 (from six-day agar) succeeded. Some gave rise to tumors with great rapidity (Figs. 4-7); others on plants of the same age and size and which appeared to be equally suitable for the inoculation gave rise to tumors very slowly (Figs. 8-10) and the tumors on several of the inoculated plants ceased to grow after some weeks and finally died (Fig. 12). All the inoculations were made into lower internodes long before the full development of the plant. Most gave teratoid tumors. The teratoid elements in these were abortive leafy shoots. No flower buds developed and no roots from any of these tumors, but frequently roots were stimulated to grow from the stem below the tumor both in these (Fig. 13) and in the subsequent inoculations. None of the leafy shoots that developed from these tumors were able to maintain the physiological functions of the plant. These were cared for by one or two strong shoots which developed normally from the lower leaf axils after the top was removed for the inoculation and considerably in advance of the appearance of the tumors. The tumors grew freely from all inoculated parts of the cut surface except the pith, but, so far as could be determined without making sections, the teratoid elements developed exclusively in tumors situated over the junction of wood and pith, *i. e.*, over the inner phloem region (Figs. 15-17); but not enough sections were cut to determine in every case their exact origin. In one plant (Fig. 18) two teratoid tumors were found to be outgrowths of the cambium. It is fairly certain that none of the many cortex tumors developed any teratoid elements unless it be the one shown at the left in Fig. 18. The leafy shoots grew out of the substance of the tumors, not out of the stem in their vicinity, and many of their leaves were defective in various ways (Fig. 6). All of these plants were in pots, but were vigorous and free from insect and fungous parasites.

II. *Inoculations of July 7.*—The inoculations of July 7 were from four-day agar cultures and were on taller, ranker plants which had rooted through the bottom of the rather small pots into a deep central bed. The cut internodes were softer than in Series I and some of them dried out without yielding tumors; but 15 of the 19 inoculations succeeded. In this case all the cut surfaces were covered lightly with collodion immediately after the inoculations (see Series V). The plants were from four to five feet high and nearly ready to develop blossom buds. Some of the internodes selected for inoculation were midway of these tall plants and others were near the top, but up to that time no flower buds had appeared. One of the upper inoculations yielded a teratoid tumor containing abortive flower buds as well as leafy shoots (Figs. 19, 20). The lower inoculations yielded many ordinary crown galls (sarcomas) and also teratoids in a number of instances, but the teratoid tumors contained only abortive leafy shoots, not flower buds. Here again the teratoid tumors seemed to arise from the region

of the protoxylem or that of the inner phloem, *i. e.*, the shoots were in tumors that developed over the pith periphery. The stems inoculated exclusively in the pith gave no tumors; those inoculated in the cortex yielded only sarcomas (Fig. 21). Concerning the cambium I was not so certain, because it is a narrow line on cross-section and even when working under a hand lens it is difficult in a long series of needle-pricks always to puncture that tissue only because sometimes a few minutes after it has been cut it cannot be seen clearly. The cambium tumors seemed, however, to be sarcomas, so far as one could judge origin by location in early stages of development. It is conceivable that the cambium might yield either sarcomas or teratoids, the difference depending on the particular cells inoculated, that is, on whether the infected needle entered the region of conjunctive-tissue cells or of multipotent or totipotent cells. Some of the teratoids developed shoots several inches long provided with leaves one to three inches in length (Figs. 22 and 25), but in all cases such shoots were tumefied (sarcomatous) at the base. Often on other parts of the same tumor there were close-set masses of pale-green buds (50 to 100 or more) which never developed further (top of Fig. 25). Not infrequently, both in this series and in the next, the teratoid elements over the entire tumor were of this second type and aborted very early (Fig. 27), never producing well-defined leafy shoots; nor did the tumors themselves in such cases resist decay beyond five or six weeks (Fig. 28, top row). Even in the tumors which grew rapidly and developed luxuriant leafy shoots there was always something wrong with the latter, *e. g.*, they grew rapidly for a short time only, were swollen at the base or throughout (*i. e.*, contained sarcomatous tissue), or were monstrous (distorted and fused with other shoots), feebly vascularized, pale green, and unable to develop beyond a soft, young stage. The best of these shoots died within three or four months, and decay of the body of the tumor soon followed. Often decay of central portions set in much earlier (Figs. 23 and 26 and tumor of the main axis on Fig. 29).

The flower buds which developed out of the tumor (Figs. 19, 20) contained stamens and pistils, but none of them came to maturity. All the buds dropped off one by one before the corolla opened.

In every plant, as in the first series, a new top was developed out of normal buds lower down, the leafy shoots in the tumor not being able to serve the needs of the plant. Some of these new tops were used for the third set of inoculations.

III. *Inoculations of July 29.*—The inoculations of July 29, being high on the plants, which were now in blossom, many teratoids bearing abortive flower buds were expected, but only leafy ones were obtained, that is, although there must have been "flower stuff" in the main axis at or near the level of the origin of these shoots it did not enter into them, the latter, at least where inoculated, containing exclusively "stem stuff" and "leaf stuff." The branches to be inoculated were cut at about midway of their length, in the middle of internodes as before. The 15 inoculations were by needle-pricks from two-day agar cultures. All succeeded. Nearly all gave teratoids, and most of these grew rapidly (Figs. 28, bottom, and 29,

top), but two or three lagged far behind the others for no apparent reason, the plants being equally well developed. This contrast in amount of growth was well shown at the end of five weeks in two plants inoculated on the same date from the same culture and growing side by side, both tumors being teratoids, but one a thousand times as large as the other. It was also shown conspicuously in other plants (see Fig. 32, made toward the end of the seventh week, where only the larger tumor is a teratoid).

Here also in several instances, as was clearly visible in early stages of growth, the tumors bearing shoots were exclusively those which developed over the region of the pith periphery, but not enough sections were cut to be certain of their exact origin.

As in the second series, two types of teratoids grading into each other appeared. In the one type several relatively large, soft shoots developed along with several to many smaller ones (Fig. 28, V). In the other type there appeared no large shoots, but several hundred small shoots—distinct pale green centers of growth which were all of about the same size and which seldom passed beyond the stage of buds (Fig. 28, IV). On the surface of one tumor of this type 469 of these abortive shoots were counted and one lobe of this tumor is shown (enlarged) in Fig. 30 and a stained section of it containing numerous centers of embryonic growth in Fig. 31. As in Series II, both types of shoots frequently occurred on the same tumor. The rapid decay of these soft tumors is also illustrated in Fig. 28 (made September 13) where the upper row shows three dead tumors of Series II (68 days), and the lower row, two living ones of Series III (46 days).

IV. *Inoculations of August 1.*—The inoculations of August 1 were done at the same time, in the same manner, and from the same cultures (six-day agar) as the second series on *Pelargonium*, and were in the same hothouse. They were done on the tops of five tall, rather spindling (crowded) firm tobacco plants rooted through the bottom of the pots into a central bed and not yet in blossom. They were in two lots:

(1) Five main axis cross-cut internodes were needle-punctured on the cut surface in various tissues.

(2) Five cut midribs were needle-punctured in various tissues of the cut end which was within an inch or two of the junction of the leaf with the stem.

Results.—On September 15 (46th day) the results of the inoculations were as follows:

(1) *Stems.*—Two failed; three produced minute tumors. One of the internodes showed six very small tumors from as many needle-pricks, two of which were teratoids.

(2) *Midribs.*—All failed. The failures were due, I think, to early loss of turgor owing to evaporation from the cut surface.

In all respects these inoculations behaved like the out-of-door inoculations to be described later, although the plants were in the same hothouse, on the same central bed and treated in the same way as those which yielded the very successful inoculations of Series II and III. Series I was in another house.

V. *Inoculations of September 7.*—The inoculations of September 7, in the same house as Series I, were made on 28 young, clean, vigorous tobaccos standing in 12-inch pots. They were from two to three feet high with many long and broad leaves. The stems at the base were an inch or more in diameter. They were cut off for inoculation at from one to two feet from the ground, and the upper three leaves also were removed except a small part, leaving five or six big, lower leaves (a foot or more in breadth and $1\frac{1}{2}$ to 2 feet in length) to carry the plant. The cuts were in the middle of soft internodes varying in diameter from $\frac{1}{2}$ to $\frac{3}{4}$ inch, and the shallow inoculations were made from 48-hour agar streaks, the depth of the numerous punctures varying from 1 to 2 mm. This experiment was planned with special reference to determining more definitely in which tissue the teratoid tumors originate. All of the inoculations were made under a hand lens, great care being taken to puncture only selected definite areas. The plants were in fine condition and I expected striking results. The 10 plants of the west row (right side of plate) were pricked all around the cortex and in the middle part of the pith. The nine plants of the middle row were pricked in the cambium region all around, but occasionally the needle (especially its tip) may have entered a little to one side or the other of this narrow ring of tissue. The nine plants of the east row were pricked in the outer part of the pith where it joins the vascular cylinder (inner phloem region). The needle used was one having the extreme tip bent at right angles to the shaft, so that only very shallow punctures could be made and great care was taken to puncture on a line parallel with the longer axis of the internode. The cut surface was shaded from the sun during the inoculations and immediately after the wet surface was wiped dry with a tobacco leaf and covered copiously with collodion, over which tobacco leaves were placed as a screen from the hot sun until the evening of the next day. The layer of collodion curled up and fell off after a few days, but it served its purpose, namely, to keep in the moisture of the cut surface until the plant could protect itself by the formation of a cork layer across the soft pith, and also much more than its purpose as subsequent results demonstrated, *i. e.*, it not only protected the cut surface from loss of water, but also destroyed the majority of the inoculated organisms and materially changed the conditions of the experiment. Strong shoots began to develop at once from axillary buds near the top of the cut stem and were several inches long at the end of 12 days (Fig. 33), while, much to my surprise, no tumors were yet visible. Also on September 29 (22d day), no tumors were visible. Even on October 20 (end of 43d day), only one tumor was visible—a small cambium teratoid. On November 12 to 14 conditions were as follows:

(1) *Cortex.*—One tumor on each of four plants. Two of them are bursting out below rather than through the cut surface as if only the more deeply lodged bacteria had been effective.

(2) *Cambium.*—One tumor on each of three plants. Two of them are bursting out below instead of through the cut surface as is usual in such inoculations.

(3) *Protoxylem Region.*—One tumor on each of three plants. All are teratoids.

Result.—Ten tumors only at the end of 68 days and all of these very small. An astonishing result considering the vigor of the plants inoculated, the virulence of the culture and the number of needle-pricks.

The final results obtained at the end of $4\frac{1}{2}$ months were as follows:

(1) *Cortex and Pith Punctures.*—The cortex yielded five very slow-growing tumors, three of which were teratoids (Figs. 39 and 47). None of the pith punctures gave any tumors.

(2) *Cambium Punctures.*—The cambium yielded five very slow-growing tumors, all of which were teratoids (Figs. 44, 46*b* and *c*). The largest of these cambium teratoids is shown in Fig. 46*b*, and the smallest in Fig. 46*c*. The others were intermediate, but much smaller than the one shown in Fig. 46*b*, the best one being exhibited December 18, 1916, before The Johns Hopkins Medical Society and afterwards given to Dr. Winternitz. This was not photographed.

(3) *Protoxylem and Pith-Periphery Punctures.*—The protoxylem region yielded five very slow-growing tumors, all of which were teratoids (Figs. 34, 46*a*).

Considering the rapid-growing succulent nature of the stems inoculated (Fig. 33), these results were very different from those anticipated, since *out of approximately 375 needle-punctures only 15 (4 per cent) yielded tumors, and very slow-growing ones at that, while on 13 of the 28 plants no tumors whatever developed.* Moreover, the tumors started off so very slowly that for a number of weeks I thought the experiment was destined to be an entire failure. Finally, when the tumors did begin to show, they appeared first not on the cut surface as in all the previous experiments, but as swellings in the deeper parts of the tissues, *i. e.*, those remotest from the surface and farthest from the reach of the ether of the collodion; in other words the outer surface of all the needle-pricks and the depths of most of them were disinfected at the start by the excessive application of the collodion. As it finally turned out, however, the experiment is one of the most interesting in the series. Its results will be the more striking if we compare them with those of all the other inoculations detailed in this paper (excluding, of course, the slow-growing garden experiments on tobacco and the similar house experiment No. IV). We then have for comparison the following:

Tobacco experiments I, II and III—46 inoculations, 90 per cent successful.

Pelargonium experiments I, II and III—100 inoculations, 100 per cent successful.

Ricinus experiments I, II and III—75 inoculations, 100 per cent successful.

Okra experiments—25 inoculations, 100 per cent successful.

Balsam experiments—12 plants, about 50 groups of punctures, 100 per cent successful.

Tropaeolum experiments—15 inoculations, 100 per cent successful.

Brassica experiments—10 inoculations, 100 per cent successful.

Total, 321 inoculations, successful, 98+ per cent.

Serial sections from these tumors show that the teratoids may arise in tobacco either from the ordinary cambium or from a regenerative tissue at the junction of wood and pith, that is, from the region of the inner phloem, usually from its outer face (Figs. 35-38, 40-43, and 47, 48), where under the action of the parasite wood-vessels (tracheæ) are produced.

Concerning the three cortex inoculations which also gave rise to teratoids, the evidence from the sections is that two of these are developments from the cambium. It might be either that in these instances my needle wounded cambium as well as cortex, or, if not, that subsequently the overgrowth of the cortex tumor penetrated into and involved the cambium region and thus induced it to form leafy shoots. Sections from one of the tumors seem rather clearly to indicate the latter origin of the teratoid elements. Concerning the third teratoid, said to be cortical, the needle-puncture which produced it must have entered the region of the inner phloem (Figs. 47, 48), for it is that part which has proliferated.

B. IN A GARDEN.

Observations of September 14 to 19, 1916, on internodal (mostly main axis) tobacco inoculations done in August on plants growing in good earth out-of-doors on the grounds of the United States Department of Agriculture (Fig. 49).

I. Inoculations of August 1 from six-day agar.

Results.—*a. On cut internodes.* One failed, eight stems gave tumors. All were very small (under 3 mm. in diameter) and not one was a teratoid.

b. On ends of cut midribs near the stem. Five failed; three were missing.

II. Inoculations of August 5 from three-day agar, all into ends of cut internodes.

Results.—The results may be briefed as follows: Twenty failed to produce tumors; two were missing or overlooked; 22 produced from one to a dozen small tumors (1 to 2 mm. or less in diameter).

These tumors were astonishingly small (Fig. 50) in comparison with those produced on the softer and better fed plants in the houses. Of these 22, only five produced teratoid elements (tiny green shoots) as follows:

a. No. 16. Plant inoculated high up for blossom teratoids.

b. No. 21. Inoculated in protoxylem region. One small tumor has developed. It is clearly a teratoid (shows tiny green leaves), and just as clearly it is now growing well within the vascular ring (Fig. 50*a*). Longitudinal sections of the stem bearing this tumor were made and these show the vessels of the tumor to have their origin from the inner phloem region of the stem (Fig. 51).

c. No. 27. Marked "Inoculated mostly in cambium." It bears an interrupted ring of 12 tiny tumors (probably from as many needle pricks), two of which are teratoids, *i. e.*, bear minute green shoots. These two tumors are the innermost ones (top and bottom of third stem in first row of Fig. 50).

d. No. 39. Marked "Inoculated in the cambium, approximately." Bears several small tumors among which are three tiny teratoids which seem to arise from the cambium.

e. No. 43. Inoculated in the protoxylem region. One tiny tumor which bears a green shoot is well within the vascular ring. Longitudinal sections show this tumor to have originated from the inner phloem region. A smaller teratoid tumor on the opposite side of the stem arises from the cambium; a third very small tumor which is not a teratoid grows from the cortex (conjunctive tissue). Not photographed.

The most striking result of this experiment, as of the preceding, is the insignificance of the tumors considering the time that has elapsed (six weeks) and the size of the plants which are leafy and six to seven feet high (Fig. 49).

I cannot help thinking, not only as a result of these experiments, but also of many others, that over-nutrition with its resultant rapid growth and soft tissues greatly favors the development of these tumors, whereas moderate feeding, which induces a slow firm growth, discourages them. They do not occur in the absence of the bacteria.

EXPERIMENTS ON PELARGONIUM.

When it had been settled that atypical teratoid tumors could be produced from the midribs and the internodes of tobacco, I turned my attention to the leaves and internodes of the common cultivated geranium (*Pelargonium zonale*) selecting a double, red-flowered variety which had previously given teratoids abundantly when inoculated in the leaf axils (Fig. 52).⁵ All of the plants used for these internodal inoculations were hothouse-grown specimens and were in good condition, free from insects and fungous parasites. My first inoculations were made on July 7, my second on August 1, and my third on September 29.

I. Inoculations of July 7.—The first plants used were rather tall, straggling plants inclined to produce foliage rather than flowers, since they stood on a central bed and their roots had grown through the bottom of the pots into the deep earth. The inoculations were made on the cut surface of internodes at the same time, in the same manner, and from the same cultures (four-day agar) as in the second series of tobaccoes. The stems were cut off well toward the top of the plant (about two feet from the ground) and were inoculated in the pith as well as in the other tissues, since I wished to know whether the young pith would proliferate. All of these 18 internodes gave tumors freely over the whole or nearly the whole inoculated surface including the pith, and most of them were teratoids, leafy shoots, however, being more abundant in them than floral abortions, although in places sparingly four of them developed small, irregular outgrowths showing the red color of the flowers. Photographs of several of these teratoids are shown in Figs. 53, 54, 56 and 57. None of the teratoid elements was developed out of the pith, and none, I believe, came from the cortex or from the protoxylem region, there being no inner phloem in the Pelargonium. Of the whole number of inoculations into shoots none failed, but some of the tumors grew

⁵ See also *The Journal of Agricultural Research*, April 24, 1916, Plate XVIII; and *The Journal of Cancer Research*, April, 1916, Plates XIV and XV.

slowly, *e. g.*, Fig. 55, which showed no teratoid elements. In the two stem ends which were sectioned in early stages of the tumor-growth, the teratoid elements clearly were developed from the cambium, while the non-teratoid tumors on the same stem were from the cortex, or cortex and cambium (Figs. 58 and 59). In nearly all of these teratoid tumors there was more or less fasciation of the leaves and shoots. See, for instance, the tallest leaf in Fig. 54*a*, the blade of which is fused into a cup. Generally about two months after their appearance, but sometimes earlier, the teratoid elements died (Fig. 54*b*), and the tumors themselves soon after softened centrally and rotted. No definite flower buds appeared such as those shown in Fig. 19, but only numerous tiny, twisted outgrowths containing the red flower pigment. In other respects, *i. e.*, except for the occurrence of pith proliferation and the absence of normally formed flower-buds, this experiment duplicates in all respects the corresponding one on the tobacco and shows that teratoid tumors full of abortive leafy shoots and exhibiting variable rates of growth can also be produced from the cut internodes of the *Pelargonium*, *i. e.*, from places where normally no shoots ever appear. Roots, however, grow out of such cut surfaces if they are buried in the earth, and this is the gardener's method of multiplying geraniums (Fig. 63).

II. *Inoculations of August 1.*—The second experiment was in all respects a duplication of the first, and was done on the same group of plants. The results were the same, to wit, the pith as well as other portions of each one of the 16 inoculated internodes proliferated, the whole top being covered and overgrown with tumor tissue (Figs. 60 and 61). All not only contracted the disease, but all produced abortive leafy shoots and five also produced red pigment (flower color) in places. One of these red patches (back of No. II, Fig. 60) was cut out and fixed on September 6 and afterwards sectioned and photographed (Fig. 80). All were cut early (September 13) and photographed on one plate (Figs. 60, 61), at which time (44th day) all but one (No. VIII) were living.

The teratoid elements grew slowly as compared with those on the tobaccos of Series I, II and III, and often a considerable period elapsed before they became evident, *i. e.*, there was not much evidence of green leafy shoots in these tumors until about the beginning of September (30 days). None of these shoots developed from the pith, most were well out toward the periphery of the tumor (cambium region). Frequently there was more or less fusion of neighboring parts normally separate (fasciation). See, for example, Fig. 61, XVI, where the photograph shows a fused twisted petiole, bearing two leaf-blades. The same kind of fusion occurs at X on Fig. 60, VI, but is not distinct in the photograph. Tumors II and III on Fig. 60 and XI on Fig. 61 also bear fused masses of leaf buds comparable to those which appeared on some of the tobacco teratoids, *e. g.*, Figs. 1 and 25.

III. *Inoculations of September 29, 1916.*—The third experiment was made exclusively on young leaves (blade and petiole) to see if teratoids could also be obtained from these

parts, as had been done on tobacco.⁶ About a dozen leaves were inoculated and six of them produced small tumors bearing leafy shoots. One was on a petiole (Fig. 62) and the others were on the leaf-blade. The best developed were picked off by some one before photographs had been made.

In Fig. 63 are shown crown-gall teratoids, or what I believe to be such, occurring naturally on two *Pelargonium* cuttings. These originated on the propagating bench of a florist's establishment near Baltimore and were received in March, 1917, through the courtesy of Mr. Philip Garman, of the Maryland Agricultural Experiment Station. Poured plates were made from the base of Plant I after surface treatment with mercuric chloride, and white colonies were obtained on agar-poured plates which appeared to be crown-gall colonies, that is, they looked typical. Five of these were selected, subcultured, and inoculated into *Ricinus*, *Pelargonium* and tobacco, but all failed. Had we been less certain at the start we would have subcultured from a much larger number of colonies and then very likely some of them would have proved infective. The writer has used *Pelargonium* for crown-gall inoculations many years, but this is the first time any natural tumors have been seen on the plant. In both instances the tumors started from the base of stunted cuttings, *i. e.*, in the knife wound, and probably from contact with infected soil. The tumor on No. II has developed both roots and shoots.⁷ Further details on *Pelargonium* tumors will be given under "Inner Structure of the Teratoids."

EXPERIMENTS ON RICINUS.

The experiments on *Ricinus communis*, the common castor oil plant, are a continuation of those mentioned in *The Journal of Agricultural Research* (April 24, 1916), as just begun. Inoculations I and II were all done into the leaf axils and most of them developed teratoids, but always with fewer shoots than those on the tobacco or *Pelargonium*. The tumors grew with great rapidity to a diameter of several inches, decayed early, and were very destructive to the plants. The inoculations mentioned under Series III were done on young leaf-blades. Owing to the ease and certainty of inoculations and the short time required to grow plants from the seed, *Ricinus communis* is a good plant both for demonstrations and for controls when working on untried species, provided it can be grown under good hothouse conditions.

I. *Inoculations of March 17, 1916.*—These were by needle-pricks introducing the hop strain of *Bacterium tumefaciens* (from four-day agar streaks) which had been passed through

⁶ For midrib and other rib teratoids on tobacco leaves, see especially *The Journal of Agricultural Research*, April 24, 1916, Plate XXIII and text; but also *The Journal of Cancer Research*, April, 1916, Plates XIX, XXI, and XXII.

⁷ Two months later, another galled cutting was obtained from the same source. Plates were poured and a small number of colonies appeared. Twelve of these colonies, which looked entirely typical for the crown-gall organism, were sub-cultured and each inoculated into several plants of *Ricinus* and *Pelargonium*, but without positive results.

sunflower in 1915. All were successful, but I shall not here take the space to describe them in detail. The nature of the results obtained are shown substantially in the three photographs (Figs. 64 to 66) including occasional formation of roots on stems below tumors (Fig. 65). On the plant shown in Fig. 66 there was, on the tumor at the left, a conspicuous crowding, stunting, and fasciation of leafy shoots. These tumors, like the okra tumors, to be described later, were first covered with cortex, but later the sarcomatous elements ruptured to the surface conspicuously, as at *x*, *y*, *z* in Fig. 66. In Fig. 64, at the right, a portion of the teratoid growth of the tumor has become sarcomatous (petiole at *x*, and below *x* in its interior).

II. *Inoculations of March 21, 1916.*—These plants were of the same age as those in Series I and were inoculated in the same way with the same strain of the crown-gall organism, a four-day agar-streak culture being used. All the inoculations were successful, most yielded teratoids, and the disastrous effect on one of the plants is shown in Fig. 67. These two plants stood in the same pot, were of the same age and size when the left-hand one was inoculated, and the subsequent difference in behavior is to be ascribed solely to the effects of the inoculation, *i. e.*, to the development of the two tumors. Many of these tumors also were smooth at first, *i. e.*, covered with a normal membrane (epidermis) and with normally arranged subepidermal tissues, but afterwards the rough sarcomatous element ruptured through just as shown in Figs. 64 and 66.

III. *Inoculations of March 21, 1916.*—This experiment was an effort to produce teratoids from the leaf-blade of *Ricinus*. The leaves were punctured with the infected needle when young, especially in the middle of the blade where it joins the petiole. Many tumors developed but none of them bore shoots. This is, however, only a single series and the inoculations should be repeated many times, especially on very young leaves before we may conclude definitely that teratoids cannot be produced from the leaves of *Ricinus*, especially as cells capable of such growth appear from the preceding experiments to be much less abundantly distributed in *Ricinus* than in tobacco or *Pelargonium*.

It was one of the leaves in this series (collected May 19) that yielded the tumor-strand referred to in my paper in *Science* (*Science*, n. s., Vol. 43, p. 886). A cross-section of this tumor-strand 9 cm. below the primary tumor is shown in Figs. 68, 69. The strand is nearly surrounded by pith, but, as in daisy, it is included in the vascular bundle, *i. e.*, it occupies the extreme inner face of the bundle, the only elements separating it from the pith being the somewhat thickened (protective) sheath (bundle sheath?) and an occasional spiral vessel torn away from its fellows by the growth of the elements of the tumor which appear to have been derived from parenchymatous conjunctive elements (medullary ray cells) lying between the spiral vessels from which, however, that is, from normal ray cells, they stain quite differently. Numerous small petiole tumors developed from this strand, but none exhibited leafy shoots or had ruptured to the surface

at the time the leaf was collected and fixed. In places there were slight penetrations of these tumors into the petiole cavity. That part of the woody cylinder of the leaf stalk adjacent to the tumor-strand, *i. e.*, on that side of the petiole was also much thickened (sextupled in diameter).

EXPERIMENTS ON OKRA.

The inoculations on common okra (*Hibiscus esculentus*) were made June 15, 1916, into the leaf axils of actively growing plants, and produced slow-growing tumors, some of which, at least, were teratoids (Fig. 70), although that element of the tumor was very feebly developed, much less so even than in *Ricinus*. They were produced with the hop strain of the crown-gall organism and are mentioned here chiefly as confirmatory of the last statement under *Ricinus* (Experiment II). Both the tumors here shown are encapsuled, *i. e.*, covered with cortex and cork, the right one entirely, the left, except in four places where the rough irregular naked sarcomatous growth has ruptured through and is fungating on the surface. Necrosis has begun at *X*. Fig. 71 shows the back side of the left (ruptured) tumor of Fig. 70. The action of the micro-organisms has been expended, as sections show (Figs. 72, 73), chiefly on the wood and the pith, and growth has been very slow, but the tumor is due to the same cause as the other crown galls here shown, only in these okra tumors the plant has had the advantage and has protected itself as much as possible. No secondary tumors were observed and growth was so far along when these tumors were collected, the plants being in fruit, that it is doubtful whether the sarcomatous element of tumors like the right-hand one in Fig. 70, of which there were many, would ever have ruptured to the surface.

EXPERIMENTS ON BALSAMS.

Sometimes in Paris daisy,^{*} tobacco (Fig. 13), Brassica, Coleus, and *Ricinus* (Fig. 65), feeble roots have been observed to develop from stems in the vicinity of crown galls, and crown galls themselves bearing roots are seen frequently on the apple (as hairy root) and have been produced by us on a number of plants with an organism isolated from the apple hairy root, but the tobacco and *Pelargonium* teratoids treated of in this paper, all of which were produced with the hop strain of the crown-gall organism, *i. e.*, with an organism isolated from a hop tumor which did not bear roots, developed only leafy and floral abortions.

However, the common garden balsam (*Impatiens Balsamina*) when inoculated in the upper leaf axils with the same hop strain produced roots in abundance directly from the tumors (Fig. 74, made at blossoming time; and Fig. 75, some weeks later), so that here is unexpected confirmation of the view which I expressed in 1911,⁹ that "hairy root" is not due to a distinct micro-organism, but is only a special kind of crown gall, the appearance in the tumor of roots being de-

^{*} Bacteria in Relation to Plant Diseases. Carnegie Institution of Washington, Vol. II, Fig. 26.

⁹ Bulletin 213, Bureau of Plant Industry, U. S. Dept. of Agriculture, page 157.

pendent on the infection either of the root anlage or of areas containing "root stuff." Some of these balsam teratoids also bore leafy shoots (Fig. 74, at *x*; Fig. 75, at *x* and *z*), and all apparently contained "flower stuff," judging from the color of the tumors which were red (roots included) on a pale green stem in all the varieties yielding pink, red or purple flowers, but not in those yielding white flowers. In this way it was possible to tell in advance of the development of blossoms whether the plant would produce white or colored flowers. Judging from these inoculations, balsams in all of the above-ground parts must be very abundantly provided with "root stuff" or with pluripotent cells capable of growing into roots, much more so than tobaccos or Pelargoniums. Also under the stimulus of the micro-organism of crown-gall, as in Pelargonium, the floral color is anomalously distributed in the tumor, *i. e.*, it is generally diffused in the stem and root cortex. Common tobacco also has pink or reddish flowers, but I have seen no such abnormal distribution of floral color in its teratoids.

EXPERIMENTS ON TROPÆOLUM.

On August 5, 1916, a set of inoculations was also made into the common garden nasturtium (*Tropæolum majus*) with the hop strain of *Bacterium tumefaciens*, the inoculations being made into leaf axils (foreground of Fig. 49). These plants produced numerous tumors where they were inoculated and some, at least, of these tumors developed both roots and shoots (Figs. 76 and 106).

EXPERIMENTS ON BRASSICA.

These experiments were on cabbage plants and cauliflower plants grown in the hothouse. Into these plants, generally believed to be derived from the same species (*Brassica oleracea*), inoculations into the leaf axils were made on September 29, 1916, the hop strain of the crown-gall organism being used; and tumors containing both shoots and roots were obtained. The shoots from these tumors were twisted, abortive, and swollen at the base, or sometimes sarcomatous throughout, and were generally whitish or with only a little leaf green. The appearance of an inoculated stem of cabbage bearing two tumors is shown in Fig. 77, and both the front and back view of an inoculated stem of cauliflower is shown in Figs. 78, 79.

INNER STRUCTURE OF THE TERATOIDS.

The Pelargonium embryomas were the first discovered and up to this time they are the only ones that have been sectioned freely in series. The illustrations and comments, therefore, under this head will be confined mostly to the geranium, the equally interesting inner structure of the tobacco, balsam and other teratoids being left for future consideration.

With the exception of one internodal tumor (Figs. 80-87) the tumors used for these sections were axillary teratoids (like that shown in Fig. 52) and were produced by pure-culture inoculations, made in October, 1915, with the hop strain of *Bacterium tumefaciens*.

The material for the sections was collected February 28, 1916, fixed in Carnoy's solution ($\frac{3}{4}$ ethyl alcohol, $\frac{1}{4}$ glacial acetic acid), embedded in paraffin, sectioned in series on the microtome, and suitably stained and counter-stained, generally a long time with methyl green for the woody parts and then a short time with acid fuchsin (for the parenchymatous parts).

In some cases in the depths of the Pelargonium tumors I have seen what I take to be floral anomalies, in other cases I have not identified the fragments, and in still others they are clearly vegetative (leafy) parts. These parts are frequently lined with membranes and lie unconformably in other tissues, often sidewise or upside down, as may be seen from the photomicrographs. These embryonic fragments all lie in the abnormally thickened cortical part of the tumor, never in the pith or xylem region, so far as observed. They have been seen in all stages of development. Whether on the surface or buried, these teratoid fragments are usually small, and they are not malignant except in the sense that they are under an abnormal and evil stimulus due to the rapidly proliferating, unripe sarcoma cells. Wherever situated, they are in all respects like other (normal) embryonic organs, except that they are fragmentary, as if cut off and displaced by the growth of the tumor, are very feebly vascularized, imperfectly nourished, and subject to early decay. Their embryonic nature is also shown by the small size of their cells, as compared with mature cells of the same sort of tissue, by their rich plasma, by their deep reaction to stains, and by what they develop into, all of which is evident on the photomicrographs. In any stage they are easily distinguished from the sarcoma by their unlike behavior toward stains and by their regularly co-ordinated cell structure. In the orderly arrangement of their cells the elements of the embryonic tissue in these tumors may be likened to the elements of a brick wall, whereas the elements of the sarcoma are almost as disorderly as those of a fallen wall (Figs. 38, 105). In some cases where two or three of these epidermal fragments come together with a small cavity between them, as in Figs. 90, 96, 97, they are somewhat suggestive of cysts.

Fig. 80 shows a vertical section through a Pelargonium teratoid produced on the cut surface of an internode by needle-pricks introducing *Bacterium tumefaciens*. The outer surface of the stem is at the left and the arrows indicate approximately the level of the cut surface, below which for a short distance there is a disturbance in both the cortex and the pith, but the principal development of the tumor has been from the region of the vascular bundle and both phloem and xylem are involved in it, the wood in particular being much thickened. The protoxylem region is not disturbed, nor is the deeper pith or cortex. At the top are teratoid elements. Many sections were cut through this tumor, which in this region showed floral color, and details of them at various levels are here shown, *e. g.*, Fig. 81 shows thickened and distorted cambium in the deeper part of the tumor, the outermost tracheæ (xylem vessels) being at the right and the sieve tubes (phloem) at the left.

Fig. 82 is from the same section but nearer the surface, *i. e.*, in the cortex of the tumor. It shows one of those nests of twisted cells and vessels that in crown gall so commonly take the place of the normally oriented tissues—a whorl of tissues with changed cortex cells at the center, curved tracheæ midway, and bent sieve tubes on the periphery. In crown galls on various plants, *e. g.*, the peach, these pearl-like nests of woody whorls can be shelled out of the soft surrounding parts of the tumor as smooth, irregular, hard nodules, round or more often tapering to a sharp point (first described by Toumey). Fig. 83 shows two smaller immature whorls of the same sort located one field of the microscope above Fig. 82.

Fig. 84 shows a lump of deep-staining sarcomatous tissue (with distorted tracheæ) lying in more or less disturbed cortex and connected by a coarser rather vague pedicle of cells (lower side and better developed in another section) to the main body of the sarcoma.

Fig. 85, from the same vicinity, shows in its center (white area) the beginning of tumor disintegration. The central cells in this area were shriveled and the surrounding ones dead at the time the material was fixed. This area has stained a feeble greenish white, but has no power to fix the red fuchsin stain. Fig. 86 shows sarcoma cells enclosing an island of unchanged (?) coarse-celled tissue (cortex?), near the surface (top) of the tumor. The cells are much larger than those of ordinary cortex. Fig. 87 gives another portion of the sarcoma showing the small size and loss of orientation in its cells. This lies in the middle of the tumor and consists chiefly of rapidly dividing parenchyma cells among which are a few distorted vessels (tracheæ). The ratio of nuclear matter to cell cavity in normal cortex cells of tobacco or geranium is about as 1:500, but in rapidly dividing sarcoma cells, that is, in cells which cannot mature before another division occurs, the ratio is greatly reduced, being only about 1:20 or 1:30. In other words, the volume of nuclear material is greatly increased in the sarcoma.

Fig. 88 is from a solid axillary embryoma. It is a planar enlargement of a considerable fragment of the tumor, *viz.*, of a whole microtome section, the surface of the tumor being at the left. The curved part from the center (*XY*) to the left represents the overgrown cortex in which, at or near the lettered places and elsewhere, are located the embryonic fragments, photomicrographs of some of which are shown in Figs. 90 to 99, Fig. 89 showing a small abortive surface organ. Many of these, as already stated, were red, *i. e.*, showed floral color. All the deeply staining parts of this section, whether lettered or not, contain embryonic tissues. Special attention is called to the fragmentary nature of these organs lying unconformably on other tissues (Figs. 90 to 92, 95), to the development of trichomes (hairs) on the epidermis of these buried fragments (Figs. 92, 94), to the orderly arrangement and characteristic staining of the component cells of these embryonic masses, and to the proximity of differently staining pseudo-embryonic and disorderly (sarcomatous) elements (Figs. 90, 92, 93).

Figs. 101 to 104, which are from another tumor, show a small tooth-shaped bud, normally arranged as to its cells, but lying bottom up in overgrown cortex and surrounded by sarcomatous elements. Especially in Fig. 105 (from the same series) the sharp border-line between sarcoma and overgrown, but normally arranged cortex, can be seen most beautifully. Figs. 101-104 and Fig. 105 are details of Figs. 65 and 64 in my paper in *The Journal of Cancer Research*, April, 1916, there insufficiently magnified, but which may be consulted for orientation. Fig. 105 is taken from the right side of Fig. 64 along the border-line of *B-B*. In Fig. 100, for comparison with 101, is shown the normal cortex of the *Pelargonium* stem covered with cork.

In Fig. 101 is shown the surface layer (enlarged cortex) of an embryoma covered by a membrane (epidermis) and bearing (at this level) five trichomes. It is a part of the tumor, *i. e.*, of the overgrowth, and its cells are smaller than the normal cortex cells, but they are arranged in an orderly way and are non-malignant except perhaps the deeper and dark-stained ones. One field of the microscope below this section (deeper in the tumor) is presented in Fig. 102, in the middle of which is the tooth-shaped piece of tissue (bud) covered with a membrane and having in its center embryo vessels, but with its apex pointed directly away from the surface of the plant, *i. e.*, toward the center of the tumor, the impulse to this abnormal development being lodged in the surrounding bacterially occupied sarcoma cells shown in the following plates (Figs. 103 to 105).

RECAPITULATION OF CROWN-GALL INVESTIGATIONS (As Related to Cancer).

(1) Crown gall is a common tumor due to a white rod-shaped polar-flagellate schizomycete. It occurs on many kinds of plants, wild and cultivated, but chiefly on the latter.

(2) In certain striking ways, as I have previously pointed out, this tumor resembles malignant animal tumors.

(3) For earlier literature on its structure and etiology, and on the morphology and biology of the organism causing it, consult Bulletins 213 and 255 of the Bureau of Plant Industry, U. S. Department of Agriculture (price 40 and 50 cents), to be had from the Superintendent of Documents, Government Printing Office, Washington, D. C. In the *Journal of Cancer Research* (April, 1916) I have specially summarized my conception of its relation to human cancer, and in *Science* (n. s. June 23, 1916), I have endeavored to answer various objections to my views.

(4) The commonest form of the tumor is a sarcoma, that is, a hyperplasia developed out of conjunctive tissues. In 1906, for the first time, this tumor was produced with a definite micro-organism by the writer and his associates, since which time we have produced hundreds of crown galls with pure cultures of our *Bacterium tumefaciens*. Cancers occur, therefore, if my interpretation is correct, not only in animals, but also in plants.

(5) The parasite is intracellular and invisible, or at least very hard to demonstrate in tissues,¹⁰ but can be isolated by the methods of the bacteriologist. It can also be isolated on slides, and stained, by diffusion in sterile water from the cut surface of fresh young tumors, and is then seen to be about the same size and shape as when grown in cultures. It is not very abundant in the tumor. It is not demonstrable in the vessels or between the cells.

(6) It does not kill the tissues, but stimulates them into abnormal growth by means of its diffusible products—acid and alkaline. (See "Mechanism of Tumor Growth in Crown Gall," *Journal of Agricultural Research*, January 29, 1917.) Death of tissues comes about in other ways, *i. e.*, by loss of water or by the destructive action of other organisms, the naked tumor offering unusual facilities for their entrance.

(7) The ordinary crown gall, as elsewhere described, gives rise to parenchymatic tumor strands on which secondary tumors develop with the structure of the mother tumor. Many of these secondary tumors have been seen especially on the Paris daisy, but so far as observed not one of them has been an embryoma.

(8) Many of the experimentally produced tumors here described are embryomas, that is, sarcomas containing rapidly developing abortive parts of the young plant—roots, stems, leaves and flower-buds or cells containing floral pigment.

(9) These tumors are caused by the same parasite as the ordinary crown galls, the difference between the two types of tumor being due to unlike reactions of the various tissues. If conjunctive tissue only is stimulated, a simple sarcoma results, but if, on the contrary, the infected conjunctive tissue cells are close to totipotent or pluripotent cells, then they also begin to grow and a complex tumor results—an embryoma.

(10) When the embryomas give rise to secondary tumors, the latter are either embryomas, like the mother tumor, or simple sarcomas. In this particular, also, they follow the law of animal embryomas (Askanazy).

(11) The organs or tissue fragments in the embryomas are feebly vascularized and abort at various stages of development, usually early.

(12) The organs and fragments of organs in these tumors are often monstrous, *i. e.*, simplified or reduced or duplicated, or fused, or abnormally oriented, or asymmetrical; and frequently their tissues also are subsequently invaded by the sarcoma.

(13) Monsters occur frequently in nature and have been produced repeatedly in various ways, *e. g.*, by grafting or by fragmentation of eggs, but are never sarcomatous or only accidentally so. This is the first time, so far as I know, that embryomas have been produced experimentally, and certainly the first time they have been produced by means of inoculations introducing a micro-organism.

(14) Whether epitheliomas and carcinomas can also be produced in plants by bacterial inoculation remains to be determined, but I believe they can be. My reason for thinking so is the fact that I have obtained the first stages of cell division in epidermal cells by bacterial inoculation and see no reason to doubt that under favorable conditions the epidermis would continue to divide and would follow its own law of growth in tumor development, *i. e.*, downward into the subepidermal tissues. This must be left for further experiment.

(15) Frequently normal tissues are torn and crushed by the enlarging tumor (mass invasion), but there is also an individual invasion on the part of tumor cells and vessels (Fig. 115). I do not know, however, whether surrounding tissues are also absorbed.

SOME DEFINITIONS.

By request, and rather against my own inclination, I give some definitions which may perhaps tend to a better understanding of my text.

Bark.—Outer part of a stem from cambium cylinder to the surface. In young stems it consists of (a) phloem, (b) phloem rays, (c) cortex, (d) epidermis. Often the cortex also contains bast fibers and collenchyma, which are strengthening tissues. In older stems the outer part contains cork and various dead tissues of a protective nature.

Bast.—The inner part of the bark. Often distinguished as *hard* bast (= bundles of tough fibers) and *soft* bast (= the phloem).

Bud.—A group of dormant cells having the potentiality of a shoot; the anlage of a shoot. Buds are commonly found in the leaf axils.

Adventitious Buds.—Buds occurring in abnormal places, usually in the absence of definite anlage, and under some special stimulus.

Cambium.—Any generative layer, as cork-cambium. Used without qualification, the generative layer encircling the wood cylinder. Wood is produced from its inner face and bark from its outer face.

Cells.—Nodal points in an organism. The morphological units of the body. Growth takes place by division of cells, but every complex multicellular organism must be regarded as one thing no matter how many cells compose it, since all its parts are physiologically coordinated. Morphologically also the individual cells are not separate entities, but are connected in many instances by delicate bands of protoplasm. As we pass downward in the scale of development the coordination is less imperative.

Unipotent.—Said of cells capable of producing only one sort of tissue, *e. g.*, connective tissue.

Multipotent or Pluripotent.—Said of cells capable of producing several tissues or a considerable part of the body.

Totipotent.—Said of cells capable of producing the whole organism.

Collenchyma.—A protecting and strengthening tissue found in the outer part of the cortex in many plants. It consists of groups of lengthened cells with thickened angles.

Conjunctive Tissues.—The connective tissues of the plant. See diagram.

Cork.—A firm, impervious, many-layered, protective tissue which takes the place of the epidermis on older stems.

Cortex.—The outer part of the living bark. The cylinder of parenchymatic cells lying between the phloem and the epidermis or its equivalent, *i. e.*, on the older stems the cork cylinder. Special cells of the cortex exhibit various secretory functions.

Embryonic.—Of or pertaining to the embryo plant or animal.

Pseudo-Embryonic Tissue.—Cancerous tissue in the broad meaning of that term. This tissue has taken on increased vegetative

¹⁰ I now think the intracellular rods which we stained by means of gold chloride, and which I interpreted as the parasite, are mitochondria.

activity, emancipated from physiological control, and at the same time has lost the ability to ripen and differentiate its cells. This is the most fundamental distinction between cancerous tissue and normal embryonic tissue.

Epidermis.—A living layer, one cell thick, covering young stems, leaves, etc. Its outer surface is protected by cutin, wax, etc. The plant equivalent of epithelium.

Fasciation.—A peculiar phenomenon not uncommon in plants, whereby a growing point flattens out as it grows or breaks up into several to many flattened fused shoots—a monstrous growth.

Germ Cells.—Those ovarian cells which, when fertilized or developed parthenogenetically, reproduce the entire organism. Possibly, also, cells or groups of cells widely distributed in the body (either normally or abnormally) and usually dormant but potentially able to reproduce the whole or a considerable part of the organism. Such cells are supposed by many persons to be the only ones capable of producing embryomas.

Giant Cells.—Cells containing several to many nuclei. Those not due to cancer are distinguished as "foreign body" giant cells, but this is probably a distinction without a difference. They are found in tuberculous nodules, in nematode galls, and in tissues reacting to the injection of various extraneous substances.

Somatic Cells.—The mass of cells making up the body of a plant or animal. All cells but germ cells. Terms used by Weissmann.

Hyperplasia.—A tumor due to increase in number of cells. All cancers are hyperplasias, but all hyperplasias are not cancers.

Hypertrophy.—An enlargement of individual cells.

Medullary Rays.—Conjunctive tissue separating the vascular bundles and, in stems of the first season, extending from cortex to pith. The silver grain of wood. It is developed from the cambium line. See radiating black lines in text figure.

Phloem Ray.—The outer, bark-part, of the medullary ray.

Xylem Ray.—The inner, wood-part, of the medullary ray.

Meristem.—Any cambium or generative layer.

Mitochondria.—Normal organs of the cell which recently have attracted much attention. They are self-motile. Often they are rod-shaped and divide like bacteria, which, frequently, they also resemble in size and in movement. Their function is unknown or still in dispute. (See a very good paper by Lewis and Lewis, in *Amer. Journ. of Anatomy*, 1915, XVII, No. 3, pp. 339-401.)

Node and Internode.—The joints of a stem. See text.

Pith.—The inner part of the conjunctive tissue. It forms the center of stems, and in old stems it is a dead tissue.

Phloem.—Technical name for the inner part of the bark cylinder. It consists chiefly of sieve tubes and companion cells. It functions as a carrier (downward) of elaborated nitrogenous slime compounds. See *R* of text figure.

Phloem Ray.—(See medullary ray.)

Plasma.—*Protoplasm*.—The living contents of the cell outside the nucleus. It consists of a clear, non-motile, fatty surface membrane (hyaloplasm) which controls osmosis, and of an interior, granular motile polioplasm. In terms of colloidal chemistry the hyaloplasm is a *gel* and the polioplasm is a *sol*.

Protophloem.—Primary soft bast. The earliest phloem.

Protoxylem.—The primary wood consisting of ring vessels or spiral vessels. The earliest xylem. See *S* of text figure.

Secondary Infection.—As here used the invasion of a cancer by some parasite or saprophyte.

Starch.—A carbohydrate storage product corresponding to glycogen in the animal. The plant converts starch into sugar to meet needs of growth, and excess of sugar is generally stored as starch. There is often much starch in crown galls just as there is much glycogen in cancers.

Stroma.—The connective tissue and vessels of a tumor. In crown gall it consists of conjunctive tissue and two types of vessels—tracheæ from the xylem, and sieve tubes from the phloem.

Stuff.—Technical term introduced by Sachs to designate hypothetical reserve substances specially adapted for development of roots, shoots, etc.

Trichomes.—The hairs of plants. These are outgrowths from cells of the epidermis. They are either simple or compound. Many are glandular at base or apex.

Turgor.—Opposite of flaccidity; the state of being full of water. Without turgor no cell can divide.

Wood.—The lignified chief strengthening and supporting part of the stem, which acts also as a conductive and aerating tissue. It is composed mostly of thickened fibers and vessels permeated with a hard substance called lignin, but it also contains more or less parenchyma. Its earliest formed vessels next to the pith periphery are ring or spiral vessels. These very soon give place in the plants here considered to tracheæ (pitted or scalariform

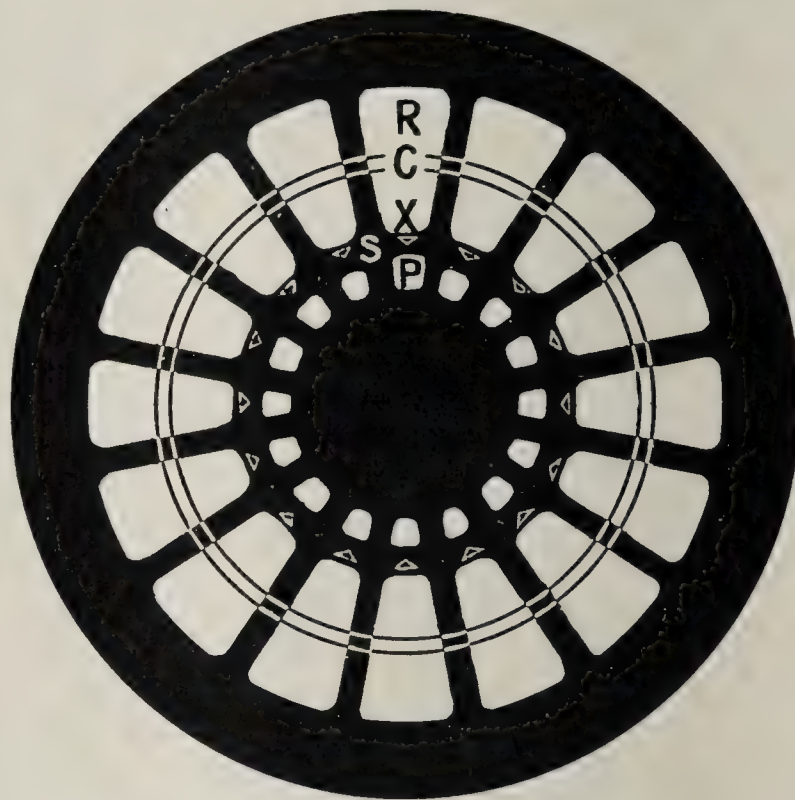


Diagram of structure of a tobacco stem (internode) in cross-section. The black center, black periphery and black radial bands represent the conjunctive tissue, while the white areas represent the general arrangement of the vascular bundles. *R*, outer phloem; *C*, cambium; *X*, xylem (wood); *S*, location of the spiral vessels; *P*, inner phloem. Teratoids may arise by inoculation either from *C* or from the outer face of *P*.

vessels), which are the only sort in the secondary wood. Tracheæ do not occur normally in cortex or pith but are produced there under the stimulus of the crown gall *Schizomycete*.

Xylem.—Technical name for the wood cylinder. It consists of vessels, wood fibers, and wood-parenchyma traversed by medullary rays. It functions not only as a support and as a carrier (upward) of water and dissolved salts, but acts also as an aerating tissue.

Cancer.—In England and France, and in my usage, which follows the common usage, the name for any malignant tumor (hyperplasia) from whatever tissue derived. Among oncologists in Germany and the United States, this term is usually restricted to carcinoma.

Sarcoma.—A fleshy, malignant tumor (hyperplasia) produced from connective tissue cells.

Epithelioma.—A flat, eroding, malignant tumor (hyperplasia) developed from epithelial cells which grow downward into the subepithelial tissues.

Carcinoma.—A malignant tumor (hyperplasia) developed from the epithelium of various glands.

Embryoma.

Terms used to denote the most complex type of tumor in which, in man, the

Atypical Teratoid.

malignant part consists usually of a

Embryonal Teratoid.

sarcoma or of a glioma (Askanazy)

Solid Cyst.

mixed in with rapidly growing fetal fragments. This form is said

to be rather rare in the ovary and rather frequent in the testicle, but occurs in many parts of the body. Said also to be either malignant or not malignant. Probably still confused to some extent with the following:

Cyst.

Terms used to designate a non-cancerous

Hollow Cyst.

tumor consisting of an invaginated surface

Dermoid Cyst.

layer (ectoderm) containing epithelium,

Typical Teratoid.

hair, fat, and sometimes fragments of various organs, as bones, teeth, etc., or more rarely a very considerable part of the foetus. The commonest kind is the ovarian dermoid.

DESCRIPTION OF FIGURES.

FIG. 1.—Tobacco inoculated February 14, 1916, with *Bact. tumefaciens* (hop strain through sunflower in 1915) into leaf axils at the top of the plant when young. Below: A rough, brownish, naked crown gall from the middle of which has developed a pale green fused mass of more than 100 leaf-buds. Above: At Y in the midrib is a non-teratoid naked tumor which has ruptured to the surface. This leaf was deformed from the beginning, i. e., the midrib never had any leaf-blade on the right side. On the under surface of the leaf X is a tumor like Y, but full of leafy shoots. The tumor at Z is also a teratoid. Photo. June 2, 1916. (Natural size.)

FIG. 2.—Tobacco shoot to show size and general appearance of the cut internode (X) when ready for inoculation. At Y is the leaf axil from which a shoot would have developed. (Natural size.)

FIG. 3.—Similar shoot about 1 month later. This was a check on the inoculations of July 7, and may be taken as a type of the behavior of all the checks on the internodal main axis inoculations described in this paper. A strong sprout (X) has pushed from the leaf axil next below the cut, which has healed over normally. Photo. August 9, 1916. (Natural size.)

FIGS. 4, 5, 6, and 7.—A series introduced to illustrate the initial slow start, subsequent rapid progress and equally rapid decay of an internodal main axis (leafy) teratoid tumor on tobacco. Cut internode inoculated by needle-pricks May 31, 1916. Date of photographs: No. 4, June 27. ($\times 1\frac{1}{4}$.) Most of the growth here shown had developed during the previous 6 days. No. 5, June 30 ($\times 4\frac{1}{2}$ circa), shows numerous diminutive shoots pushing out of the tumor substance which is growing rapidly. No. 6, July 14, i. e., 17 days after Fig. 4. Tumor now covered with leafy sprouts, a few of which have reached a length of 2 to 3 inches. A normal shoot (X) from axil of the leaf Y, and corresponding to X of Fig. 3, is at the extreme left; all others are from the tumor. Many of the leaves (Z) have cleft, one-sided or otherwise defective blades. ($\times 1\frac{1}{2}$.) No. 7, same as 6 but natural size and from the opposite side where decay has begun (direction of the arrow). There is a small tumor bursting from the top of X which is a defective leaf—one lacking most of its blade. At Y is another defective leaf—the blade being reduced on the right side.

FIG. 8.—Slow-growing internodal (main axis) leafy tobacco teratoid. All of the shoots are from the tumor and there are no flower-buds. Stem inoculated May 31, 1916. Photo. August 1. ($\times 1\frac{1}{2}$.)

FIG. 9.—The same tumor as in Fig. 8, but a month later and much larger. Entire time 3 months. Necrosis has begun. All of the small shoots are from the tumor; some are dead and others are

dying. The large shoot (X) developed from a lower normal leaf axil prior to the formation of the tumor. Photo. August 31. ($\times 1\frac{1}{2}$.) The last of the teratoids of May 31.

FIG. 10.—Slow-growing internodal crown-gall tumors on tobacco. The upper tumors are teratoids, the hairy masses being small leafy shoots. The lower tumor is a sarcoma. An independent small teratoid has developed at X. Inoculated by needle-pricks May 31, 1916. Photo. August 10. ($\times 8$.)

FIG. 11.—Section through Fig. 10. The right-hand (teratoid) tumor originates from the cambium; the left-hand, which is naked and apparently contains no teratoid elements, originates from the xylem side of the cambium (the wood), which is much thickened. The tissues are *t*, *t*, embryonic (teratoid) elements; *cor*, cortex; *p*, outer phloem; *c*, cambium; *xy*, xylem; *i p*, inner phloem; *m*, pith. ($\times 8$.)

FIG. 12.—Cut surface of two stems of tobacco showing very slow-growing internodal teratoid tumors, the lower dead and the upper dying. They were slow to start and there was no growth in either for a month or six weeks prior to the date of the photograph. The openings are needle-punctures from which no tumors developed, and most, it will be observed, are in the pith. Inoculated May 31. Photo. August 18. ($\times 4$ circa.)

FIG. 13.—Internodal crown-gall teratoid on tobacco. More than 50 leafy shoots grew from this tumor. The shoot (X) developed after the main axis was removed and before the tumor grew. The influence of the tumor extends not only below in the main axis, but also into the first internode of the big shoot at the left, as shown by the budding roots (*R*, *R*), absent above and below. Inoculated May 31. Photo. June 25. ($\times 1\frac{1}{2}$ circa.)

FIG. 14.—Top view of the tumor shown in Fig. 13. No flower-buds but numerous green (leafy) sprouts out of the pale brown naked substance of the tumor. ($\times 3$ circa.)

FIG. 15.—Slow-growing crown-gall tumors on cut surface of tobacco stem (internode). Numerous small sarcomas and also five distinct centers of (leafy) teratoid growth, four of which (*t*) have originated on the inner edge of the vascular ring. The teratoid (X) near the surface is probably from the cambium. The teratoid tissue, of course, is covered with an epidermis; the sarcomas are naked. For a longitudinal section in direction of the arrows see Fig. 17. Photo. June 26. ($\times 7$.)

FIG. 16.—Crown-gall tumors on cut surface of tobacco internode. Several, small, naked tumors and at least three distinct centers of teratoid growth which are from the inside of the vascular ring. The roundish openings are needle-stabs from which no tumors developed. Stem inoculated May 31, 1916. Photo. July 3, 1916. ($\times 12$ circa.)

FIG. 17.—(a) Longitudinal section of Fig. 15 showing teratoids (*t*, *t*) arising inside the cambium line (*c*, *c*).

(b) Cross-section of a normal portion of the same stem. *Cor*, cortex; *v*, vascular ring; *m*, medulla; *o p*, outer phloem; *i p*, inner phloem. Planar enlargement from fresh material.

FIG. 18.—Longitudinal section of a very slow-growing crown-gall teratoid (leafy) tumor on cut surface of tobacco internode (right side). The growth is from the cambium and the wood is thickened. The cortex is not involved. On the left side (top in figure) is a cortex tumor. This does not involve the cambium unless sections are missing from the series, yet it contains some teratoid elements. It is probably from the cambium because the cambium and wood under it are sarcomatous and at another level the cross-cut (inoculated) surface of the stem (at X) bears a third small tumor which is a teratoid and originates in the cambium. Inoculated May 31, 1916. Collected and fixed August 18. Slide 1271-13. (Planar enlargement.)

FIG. 19.—Crown-gall teratoid on tobacco, showing flower buds. The shoot at the right (X) grew from the leaf axil bud below prior to the development of the tumor. The tumor at this date bore numerous green leaves and five flower buds, and the base of the

shoot at Y was swollen. For the appearance of this tumor nine days later when it was nine times as large, see Fig. 20. Plant inoculated July 7, 1916, on the cut surface of the main axis (internode) near the top of the plant which had not yet blossomed, but was nearly ready to develop flower buds. Photo. July 31. (Natural size.)

FIG. 20.—Same as Fig. 19. Several of the earliest flower buds, which developed stamens and pistils but never opened, have now fallen off, as at X. The position corresponds (nearly) to that of Fig. 19, made nine days earlier, but the tumor is much larger and many new teratoid elements have developed. All the remaining flower buds (b, b, b) fell off a few days later. Fasciation at f and in other places. Photo. August 9. (Nearly natural size.) There was at this time no necrosis, but decay set in a few days later, and on September 1 all of the teratoid elements were either dead or dying, and the body of the tumor was beginning to shrivel.

FIG. 21.—Crown galls on the cut stem (internode) of a tobacco plant. The inoculations were made July 7, 1916, into the cortex. A few needle-thrusts may have entered the cambium as at X, X, but none of the tumors has developed shoots, i. e., they are naked sarcomas. Nearly every needle-thrust produced a tumor. The two larger tumors at the top were of the same size as the others 48 hours earlier. Photo. July 31. ($\times 8$, nearly.)

FIG. 22.—Teratoid crown gall on tobacco. The main axis was cut off at the top of the plant in the middle of an internode, and the cut end inoculated on July 7 by means of needle-pricks from an agar streak culture of *Bact. tumefaciens*; X and Y are normal shoots which developed after the top was removed and before the tumor appeared, the top of Y being cut away at the time of making the photograph; Z, Z', are the subtending normal leaves. Tumor filled with shoots, the bases of many of which are swollen (sarcomatous). Photo. August 4. (Nearly natural size.) No necrosis.

FIG. 23.—Same as in Fig. 22, but 10 days later (38 days from date of inoculation) when wilting and shriveling of the teratoid shoots had begun, and also a decay of the body of the tumor in several places, as at a, b, where a white fungus has appeared (*Fusarium* sp.). Fasciations occur and all of the shoots are from the body of the tumor. No flower buds appeared. Photo. August 14. (Natural size.)

FIG. 24.—Crown-gall teratoid developed from the middle of a tobacco (main axis) internode. Shoots X and Y began to grow as soon as the top was removed, i. e., in advance of the tumor; Y is normal, X has become infected with internal tumors (the raised light spots) which are invasions from the primary tumor. Tumor filled with luxuriant leafy shoots. Plant inoculated on the cut surface of the internode July 7, by needle-pricks. Photo. August 1. (Natural size, nearly.)

FIG. 25.—Same as Fig. 24, but 14 days later (38 days from inoculation). The tumor has developed rapidly and in the upper part are now to be seen a multitude of closely packed pale green leaf-buds like those shown in the middle of Fig. 1. No evidence of flower buds. The larger shoots have begun to shrivel, but there is as yet no necrosis. The tumors in the big branch at the left have not ruptured to the surface. Photo. August 14. ($\times 1\frac{1}{2}$.)

FIG. 26.—Same as in Fig. 25, but 23 days later (2 months after inoculation) when all the shoots have shriveled and necrosis of the body of the tumor is far advanced. Photo. September 6, 1916. (Natural size, nearly.) For a view of the opposite side of this tumor on the same date but one quarter natural size, see lower tumor of Fig. 29.

FIG. 27.—a, b. Top view of two crown-gall teratoids produced on cut surface of tobacco internodes. The tumors contain many distinct centers of greenish (leafy) teratoid growth, but none of them has passed much beyond the stage of buds, or judging from other similar tumors would have done so later. Tumors not yet beginning to decay. Stems inoculated July 7, 1916. Photo. July 26. ($\times 3$.)

FIG. 28.—Crown-gall (main axis) tobacco teratoids. All were produced from the middle of cut internodes by needle-prick inoculations. Introduced to show rapid decay and varying types of the tumor. Nos. I-IV are alike, whereas No. V contains a mixture of large and small shoots. No. VI is the fleshy back part of No. V. The upper row represents plants inoculated July 7, and the only living tumor parts are a small portion of the top of III at X. The lower two stems were inoculated July 29, and the tumors were still free from decay. The left-hand one contained many distinct centers of teratoid growth, i. e., several hundred. For enlargement of one lobe of a similar tumor see Fig. 30. Photo. September 13, 1916. ($\frac{2}{3}$ natural size.)

FIG. 29.—Three crown-gall teratoids on tobacco internodes. The lower tumor, far advanced in decay and covered with mold (*Fusarium* sp.), is the one already shown in Fig. 26. The upper tumors are internodal inoculations of July 29, 1916. All of the leafy shoots are from the tumors. Some are swollen and distorted. No flower buds were observed and there was as yet no necrosis. Photo. September 6, 1916. ($\frac{5}{16}$ natural size.)

FIG. 30.—One lobe of an internodal (main axis) tobacco crown-gall teratoid on which there were no well-developed shoots, but 469 diminutive pale green buds, all of which were like those on the lobe here shown. Query: Did all grow from displaced "germ cells" or from normal somatic cells exposed to a special stimulus? Inoculated July 29, 1916, on cut surface by needle-pricks. Photo. Sept. 13. ($\times 7$, nearly), with Zeiss 100 mm. planar. Necrosis not begun. Material fixed for sections. See Fig. 31.

FIG. 31.—Two-thirds of a cross-section of Fig. 30 in which are 30 centers of embryonic growth. The central pale, coarse-celled tissue is cortex; the dark-stained, irregular (stringy) central tissue is the sarcoma. Methyl green and acid fuchsin stain. ($\times 18$.)

FIG. 32.—Tobacco crown galls 46 days old. The plants were inoculated on the cut surface of the main axis in the middle of internodes on July 29, at which time and subsequently they seemed to be equally good plants. They were standing side by side and developed equally vigorous tops from the side shoots X, X. No. a is a sarcoma and behind it (unseen) are two other much smaller tumors of the same sort. No. b is a leafy teratoid, the shoots of which are beginning to wither. The leaves have wilted naturally, not as a result of cutting the stem. The bulk of this tumor is 1500 times that of a. Photo. September 13. (About natural size.)

FIG. 33.—South end of one of our experimental houses showing part of tobacco plants used for Series V. Photo. Sept. 19, 1916, i. e., 12 days after the inoculation, at which time vigorous side shoots were pushing, but no tumors had appeared. (Greatly reduced.) On a bench in the background are the inoculated balsams.

FIG. 34.—Tobacco crown-gall teratoid. One of the inoculated stems of Fig. 33 at the end of nine weeks showing one small leafy tumor (X) emerging well within the vascular ring. ($\times 4$.)

FIG. 35.—Section of tobacco crown-gall teratoid (Fig. 34) showing origin of the tumor chiefly from the outer face of the inner phloem—cortex not involved. The lifted up portion (at X) is cork which formed after the stem was cut and before the tumor appeared. The wings of the arrow-shaped growth are leaves in which the palisade tissue is reversed, i. e., it is below facing the axis of support. Block 1295-41. (Planar, 50. mm.) The part under x is sarcoma; all to the left of x is teratoid.

FIG. 36.—Middle (sarcomatous) part of Fig. 35 below the surface at X. The two small right-hand lobes of the tumor have arisen from the cambium, the remainder of the tumor is from the inner phloem region. Special attention is called to the loss of polarity on the part of these cells. For an enlargement of the part designated by the arrow see Fig. 38. ($\times 75$.)

FIG. 37.—Photomicrograph from Fig. 35 but under 36, showing continuation of the sarcomatous inner phloem (the darker stained part), i. e., the bottom of Fig. 36 is the same as the top of Fig. 37. The tissues are: m, pith; ph, abnormal inner phloem; sp, spiral region of the bundle; tr, tracheæ; c, cambium; sv, outer phloem; cor, cortex; s, sarcomatous cambium. ($\times 75$.)

FIG. 38.—A detail from the middle of Fig. 36 (in direction of the arrow), showing loss of polarity in the sarcomatous cells. Pith cells (*m*) at the left; *tr*, abnormal vessels (tracheæ) developed in the tumor; *sp*, normal spiral vessels of the stem lying undisturbed at the inner border of the xylem. Section stained with acid fuchsin and methyl green. ($\times 160$.)

FIG. 39.—Slow-growing (main axis) tobacco crown-gall teratoids. Plant inoculated by needle-pricks in the middle of the cut internode on September 7, 1916. Here apparently are two tumors fused, one from the ordinary cambium, the other from a meristem developed from the outer face of the inner phloem. See Figs. 40 and 41. Photo. November 15, 1916. ($\times 1\frac{3}{4}$.)

FIG. 40.—Section through the middle part of Fig. 39, showing origin of the bulk of the tumor from the cambium. The parts are: *cor*, cortex; *p*, outer phloem; *c*, cambium; *tr*, xylem; *i p*, inner phloem; *m*, pith; *x*, level of Figs. 42 and 43. The middle part of the tumor (*s*) is sarcomatous; the outer parts (*t, t, t*) with cells arranged normally are the teratoid portions. At *i p*, there is a small tumor capping the inner phloem (see Fig. 41). Slide 1302-6. Planar, 50 mm. ($\times 10$.)

FIG. 41.—Section of Fig. 39 at one edge (slide 1302-36) showing two distinct tumors (both teratoid), one (*c*) from the cambium, the other (*i p*) from the region of the protoxylem and inner phloem. The darker parts of the larger tumor (*s, s, s*) are sarcomatous and the paler parts (*t, t, t, t*) teratoid. The interrupted dark stripes below the tumor (along the inner edge of the vascular bundle) represent the sarcomatous inner phloem, a small portion of which at the level of *X* is shown enlarged in Fig. 42.

FIG. 42.—Protoxylem region between Figs. 40 and 41 at *X*, enlarged to show changed appearance of that part of the vascular bundle. Unchanged spiral vessels (*s*) at left, to the right of which are two strands of inner phloem containing tracheæ (*tr.*) and distorted parenchyma cells (companion cells?). The body of the wood lies at the left of *s*. The large pale cells (*m, m*) are pith cells. At *st* are sieve tubes. Slide 1302-12. ($\times 160$.)

FIG. 43.—Right (innermost) phloem strand of Fig. 40 at *X*, enlarged, showing sieve tubes in the center (*st*) and well developed tracheæ on both the inner and the outer face of the strand, *i. e.*, tissues which occur normally only in the wood at the left of the spiral vessels, together with plain evidence of sarcomatous invasion as shown by multiplication and distortion of short cells. This is virtually a concentric bundle with phloem at the center. At either side are the cells of the pith (*m, m*). ($\times 210$ circa.)

FIG. 44.—Tobacco crown-gall teratoid from a main axis internodal (cambium) inoculation of September 7, 1916. At *X* there was a sprout of the same size as *Y*, which fell off in handling. Masses of green buds at *Z*. Photo. January 10, 1917. (4/5ths natural size.) Back view.

FIG. 45.—Front view of Fig. 44 slightly enlarged. Tumor very slow growing and first visible as an internal swelling (*X*) a centimeter below the cut surface (see text). Necrosis and sloughing at *Y*. Time 125 days.

FIG. 46.—*a*. Tobacco crown-gall teratoid. Main axis internodal (protoxylem) inoculation of September 7, 1916. Collected November 14, 1916. Very slow-growing tumor. (Photographed under alcohol; $\times 3$.)

b. Slow-growing teratoid from same series (Fig. 33) as *a*, but a cambium inoculation. This is the largest tumor obtained from the inoculations of September 7. Photo. January 25, 1917. ($\times 2\frac{1}{2}$.)

c. Two small, slow-growing tumors from same series as *b* (cambium inoculations of September 7). Both are teratoids and no other tumors developed on the cut surface, although the lower received 16 needle-pricks and the upper nearly as many. Time 124 days. ($\times 8$.)

FIG. 47.—Slow-growing teratoid crown gall from inoculations of September 7, 1916. Fixed December 6. Cortex at right. The

tumor originates from the region of the inner phloem (see Fig. 48). Doubtful where inoculated (inoculation said to have been into the cortex). Slide 1305-15, near margin of tumor. ($\times 17$.)

FIG. 48.—Same as 47, but a more central cut showing clearly the origin of the tumor from outer face of inner phloem (*i p*); the cambium and cortex are not involved. The tissues are: *m*, normal pith; *i p*, diseased inner phloem containing tracheæ and sarcomatous cells; *sp*, normal spiral vessels of the stem bundle; *tr*, tracheæ; *c*, cambium; *o p*, outer phloem; *cor*, normal cortex; *t, t*, teratoid elements of the tumor; trichome at *h*. (Planar, 50 mm. Slide 1305-11, $\times 70$.)

FIG. 49.—North end (about $\frac{1}{2}$) of two rows of out-of-door tobacco plants used for Series I and II of August 1 and 5. Photo. Sept. 19, 1916. Pathological houses in the background.

FIG. 50.—Whole crop (nearly) of successful inoculations of August 1 and 5 (Series I and II, out-of-door) with most of the failures. The right five of the lower row are inoculations of August 1. The remainder are those of August 5. At *X, X* are small tumors bursting out below. The first four tumors of the top row are teratoids and at *A* is one originating from the region of the inner phloem as serial sections have shown clearly. Introduced for comparison with indoor inoculations of July 29 (Figs. 28, 29, 30, and 32). The ends of all these stems, when photographed, were living but rather firm. The same cultures were used on the last five of the lower row as on the Pelargoniums shown in Figs. 60, and 61. Photo. September 19, 1916, slightly enlarged.

FIG. 51.—Section of tobacco crown-gall teratoid at *A* in Fig. 50, showing origin of the tumor from the inner face of the vascular bundle. The tissues are: *s, s*, sarcomatous elements; *t*, teratoid portion; *cor*, cortex. Slide 1286B-14. ($\times 23$.)

FIG. 52.—Pelargonium crown-gall teratoid at the end of four months. Inoculated into a leaf axil January 13, 1916, from a 3-day-agar culture of the hop strain of *Bact. tumefaciens*. The shoots from the tumor were dying or dead, *i. e.*, greenish yellow or brown. The back side of the tumor was also full of shoots. The main axis above is bent and dwarfed and has dropped four of its leaves, while several others (the lighter colored ones) are pale green or yellowing. All the leaves below have fallen except the reflexed dying one at the left. Photo. May 16, 1916. (5/7ths natural size.)

FIG. 53.—Pelargonium crown-gall teratoid—an internodal inoculation which has covered the whole top of the cut stem. The inoculation like all the others was made by needle-pricks without hypodermic injection. The tumor contains four distinct centers of green leafy growth. These parts are covered with an epidermis and are hairy, while the remainder of the tumor is naked. Inoculated July 7, 1916. Photo. August 1, 1916 (straight down). ($\times 7$ circa.)

FIG. 54.—Pelargonium internodal crown-gall teratoids. Inoculated on the cut surface July 7, 1916. (a) The whole top of the stem is covered by the tumor. There is fasciation, *i. e.*, the blade of the upper leaf is fused into a conical cup. All the shoots are living. Photo. August 9, 1916. ($\times 1\frac{1}{2}$.) (b) Another plant showing numerous leaves growing from the tumor, the larger of which have begun to wither. Two small leaves which interfered with the view were cut away from the first node below. Photo. August 24. (Natural size.)

FIG. 55.—Cut surface of Pelargonium stem inoculated July 7 and photographed August 16, 1916. The slow-growing tumors are all sarcomas, at least, no teratoid elements are visible on the surface. ($\times 6$ circa.)

FIG. 56.—Pelargonium internodal crown-gall teratoid. Showing whole top covered by the tumor and petiole at the left (*f*) fasciated. All parts living. Inoculated on cut surface July 7, 1916. Photo. August 9, 1916. ($\times 1\frac{3}{4}$ circa.)

FIG. 57.—Pelargonium internodal crown-gall tumors, sarcomatous and mixed (teratoid). Very slow growing. Cut end of stem

inoculated July 7, 1916. Photo. August 15, 1916. ($\times 7$.) Side view. Teratoids at the top.

FIG. 58.—Same as Fig. 57, but a top view. The tumors at the bottom are naked and without shoots. For a vertical section see Fig. 59. ($\times 7$ circa.)

FIG. 59.—Section of Fig. 57. Block 1267, Slide 42. At the top are the non-teratoid tumors which have developed (for the most part, at least) from the cortex. At the bottom is the teratoid which does not, or did not at first, involve the cortex, but is an outgrowth of the cambium. ($\times 12$, nearly.)

FIGS. 60, 61.—Pelargonium crown-gall teratoids. All were inoculated August 1, 1916, on the cut end of internodes, i. e., remote from buds. Each one of the 16 tumors contained teratoid elements. All but No. VIII were alive when photographed. Nos. II, III, and XI show closely set masses of buds. No. II furnished the section shown in Fig. 80. No. XVI at X shows twisting and fasciation of the petiole which bears two leaf blades. Two petioles are also fused at X on No. VI. Photo. on a W. and W. panchromatic plate September 13, some of them end on. Slightly enlarged.

FIG. 62.—Pelargonium crown galls in the middle of a leaf-stalk. The lower tumor bears a cluster of young leaves. Petiole inoculated by needle-pricks with *Bact. tumefaciens*, September 29. Photo. December 6, 1916. ($\times 3$.)

FIG. 63.—Pelargonium teratoid tumors originating naturally at X and Y on gardener's cuttings bedded in earth for propagation. The specimens came from a gardener's house near Baltimore. Both show fasciation (as at f). Roots (R) as well as shoots are growing out of the left tumor on II. Although not visible in the photograph, there is a flat tumor at Y in the base of II. Photo. March 18, 1917. ($\times 1\frac{3}{4}$.)

FIG. 64.—Axillary crown-gall teratoids on Ricinus. Inoculated by needle-pricks in two upper leaf axils March 17, 1916, with hop strain of *Bact. tumefaciens* passed through sunflower in 1915. Axis twisted; top (direction of the arrow) aborted; subtending leaves reflexed; sprouts from the tumors. The petiole is twisted swollen (sarcomatous) and a tumor has ruptured from its interior at X. This leaf collapsed a day or two later. The smoother parts of the tumors are covered with a membrane. Photo. April 29, 1916. (Natural size.)

FIG. 65.—Axillary crown-gall teratoids on Ricinus. Inoculated by needle-pricks into two upper leaf axils March 17, 1916. Stem leaves reflexed and withering. Top at X aborted. The teratoid shoot at Y has developed a small tumor. The subtending petiole at Z also bears a tumor. Both of these were at first interior growths. L is a dead leaf subtending the lower tumor. Photo. April 29, 1916. (Natural size.) Three days later the plant died.

FIG. 66.—Axillary crown-gall teratoids on Ricinus. Inoculated by needle-pricks into two upper leaf axils, March 17, 1916, with hop strain of *Bact. tumefaciens*. Main axis dwarfed and distorted but growing point not destroyed as in 64 and 65, subtending leaves reflexed (the lower one, at C, has fallen and the other, at P, is dead). The upper tumor has involved all of the internode up to the third leaf (pt) which is yellowing. At W is a mass of green buds and fused leafy shoots. Tumors encapsulated at first. Afterwards the sarcoma ruptured to the surface as at X, Y, Z. Photo. April 29, 1916. ($\times 1\frac{1}{4}$.)

FIG. 67.—Axillary crown-gall teratoids on Ricinus. Left plant inoculated March 21, into two upper leaf axils. The tumors have grown rapidly and are partly naked. The main axis has aborted and the subtending leaves are reflexed. The plant is very badly dwarfed and ready to die. The control plant is on the right. On the date of inoculation the two plants were of the same size and equally vigorous. Photo. (much reduced) April 29, 1916. Time 39 days.

FIG. 68.—Cross-section of tumor strand in petiole of Ricinus—the kind of strand that yielded only sarcomas. Inoculated by needle-pricks into the blade of the leaf March 21, 1916. Collected and

fixed May 19. Cross-section in middle of petiole 9 cm. below the blade of the leaf which bore many tumors. Wood (xy) above, pith (M) below. This tumor strand (S) gave rise to hummocky swellings at frequent intervals and all that side of the petiole was thickened, especially the wood, but none of the tumors had ruptured to the surface. Slide 1225-A-18. ($\times 52$.)

FIG. 69.—An enlargement of the center of Fig. 68, showing in greater detail the interior and the surroundings of the tumor strand. A sort of fibrous tissue (thickened bundle sheath?) surrounds it. This stains very much like the collenchyma. ($\times 200$.)

FIG. 70.—Encysted, slow-growing, crown-gall tumors on okra (*Hibiscus esculentus*). Plants inoculated June 15, 1916, by needle-pricks into leaf axils with the hop strain of *Bact. tumefaciens*. By "encysted" I mean that the right-hand tumor is entirely covered by cortex and cork, and the left-hand one also except in four places (X, Y, Z, and one place on the back) where the nodular naked sarcoma has broken through. The right tumor is sound. The left one is beginning to decay in its older part (X). No. I is a teratoid and with a hand-lens a single small sprout can be seen just below Y. No. II was also inoculated into a leaf axil, but it gives no external evidence of being a teratoid. At W, a ripe fruit was cut away. Photo. September 22, 1916. ($\frac{4}{5}$ ths natural size.)

FIG. 71.—Same as I of Fig. 70, but from the back side. The lettering is the same. Z is a naked, rapidly proliferating, sarcomatous mass, but C is cortex covered by a cork layer. There is also a small naked portion behind the branch B. Photo. September 22, 1916. ($\times 2$, nearly.)

FIG. 72.—Cross-section of an unruptured okra tumor from same series as Fig. 70, showing that the bulk of the bacterial energy has been expended on the wood and on the pith, which is full of distorted fibro-vascular elements. The cells of the greatly enlarged cortex are normally arranged and not sarcomatous. The black spots in the cortex are deep-staining mucilage glands. The tissues are: m, pith; xy, wood cylinder; ph, phloem; cor, cortex; c, cork layer; camb, cambium line; tr, tracheæ and other tissues which are inclined at a right angle to the general direction of the vessels of the wood. ($\times 10$ circa.)

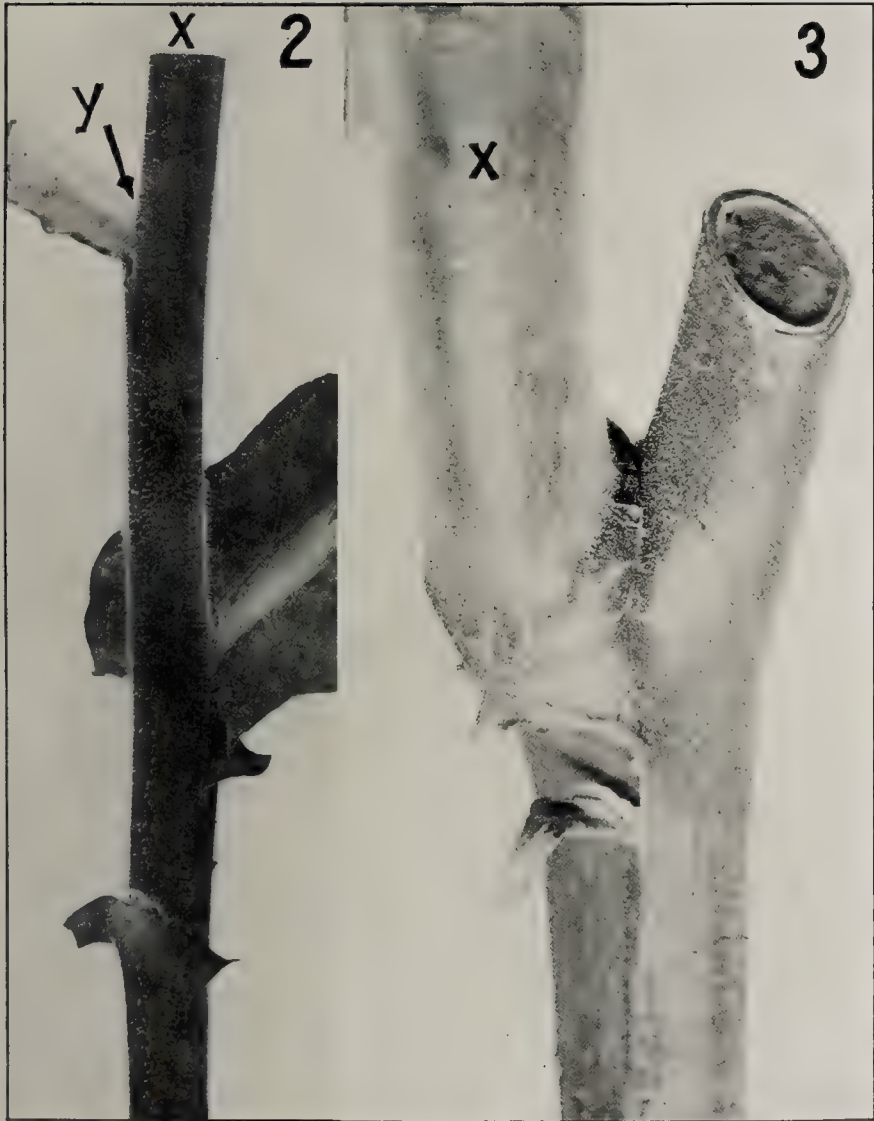
FIG. 73.—Detail from Fig. 72 at X, showing modified pith-cells traversed by distorted fibers and vessels. ($\times 68$.)

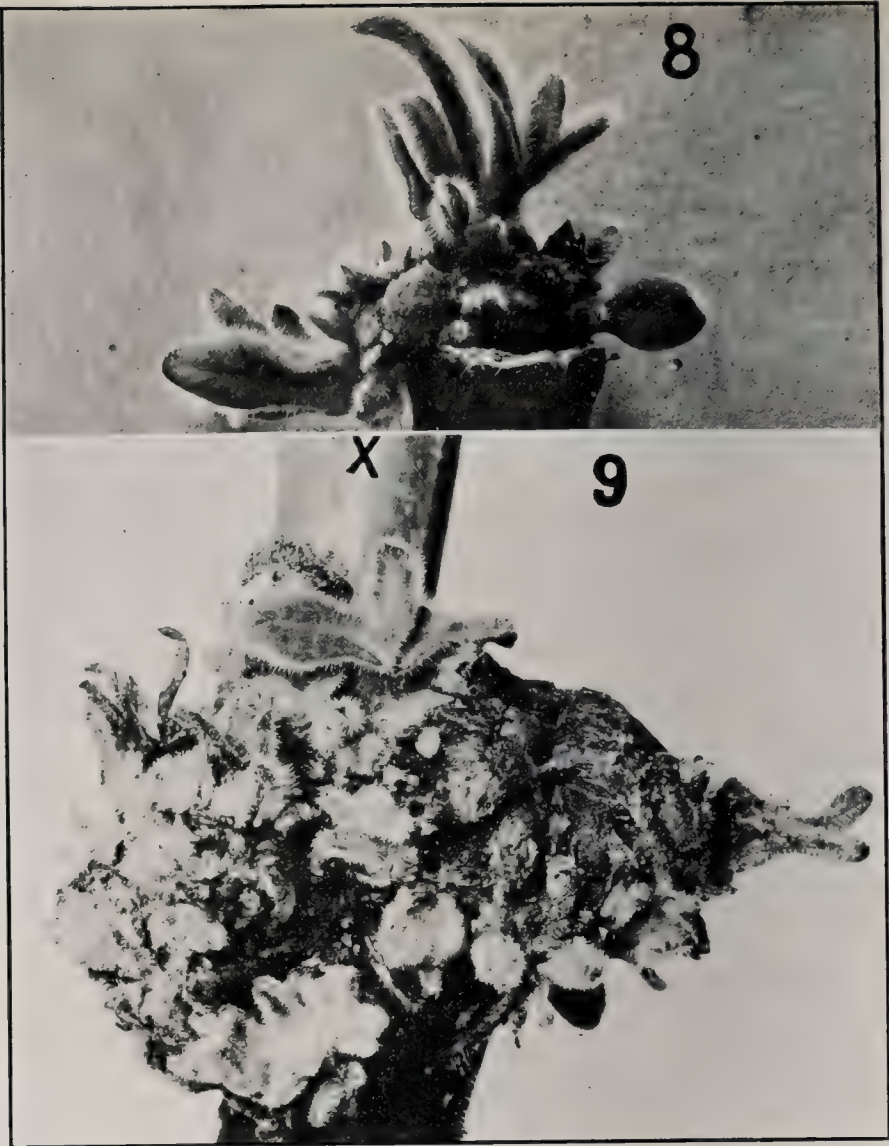
FIG. 74.—Axillary crown-gall teratoids on the common garden balsam (*Impatiens Balsamina*). Inoculated July 26, 1916, with the hop strain of *Bact. tumefaciens* in the leaf axils prior to the appearance of branches. Plant just beginning to blossom. The tumors contain roots (R), sarcomatous leafy shoots (X) and flower stuff. Photo. August 15, 1916 (natural size, on a W. and W. panchromatic plate with a red screen. The stems were actually pale green and the tumors red).

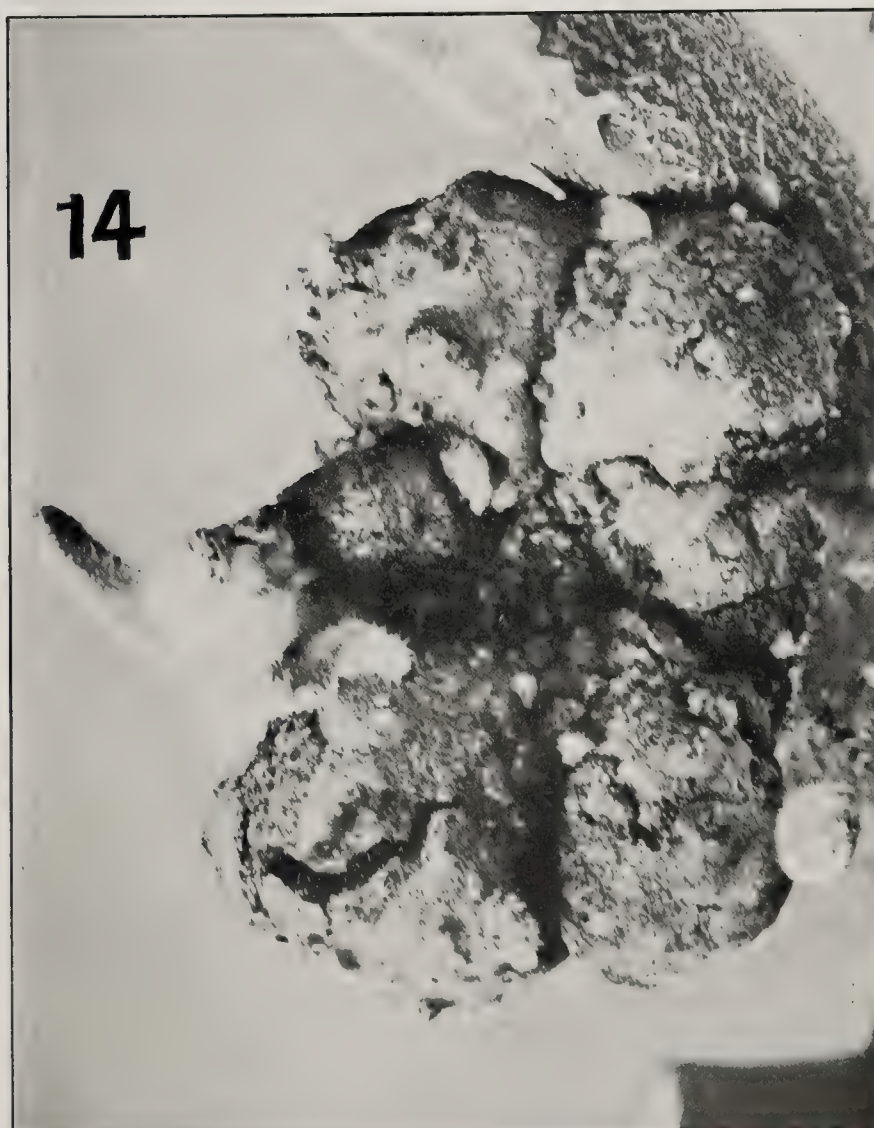
FIG. 75.—Same series as in Fig. 74, but farther along in development. The top is dwarfed and diseased branches have developed. The tumors are red (with flower stuff), roots are growing from them freely, and in two places (X, Z) small leafy shoots are visible. The distorted leaf Y also shows internal and ruptured tumors. Inoculated July 26, 1916. Photo. September 19, 1916. (Natural size.) The top of the plant extends only 2 inches above the part here shown and the diameter of the stem immediately beyond the tumor is only $\frac{1}{8}$ inch.

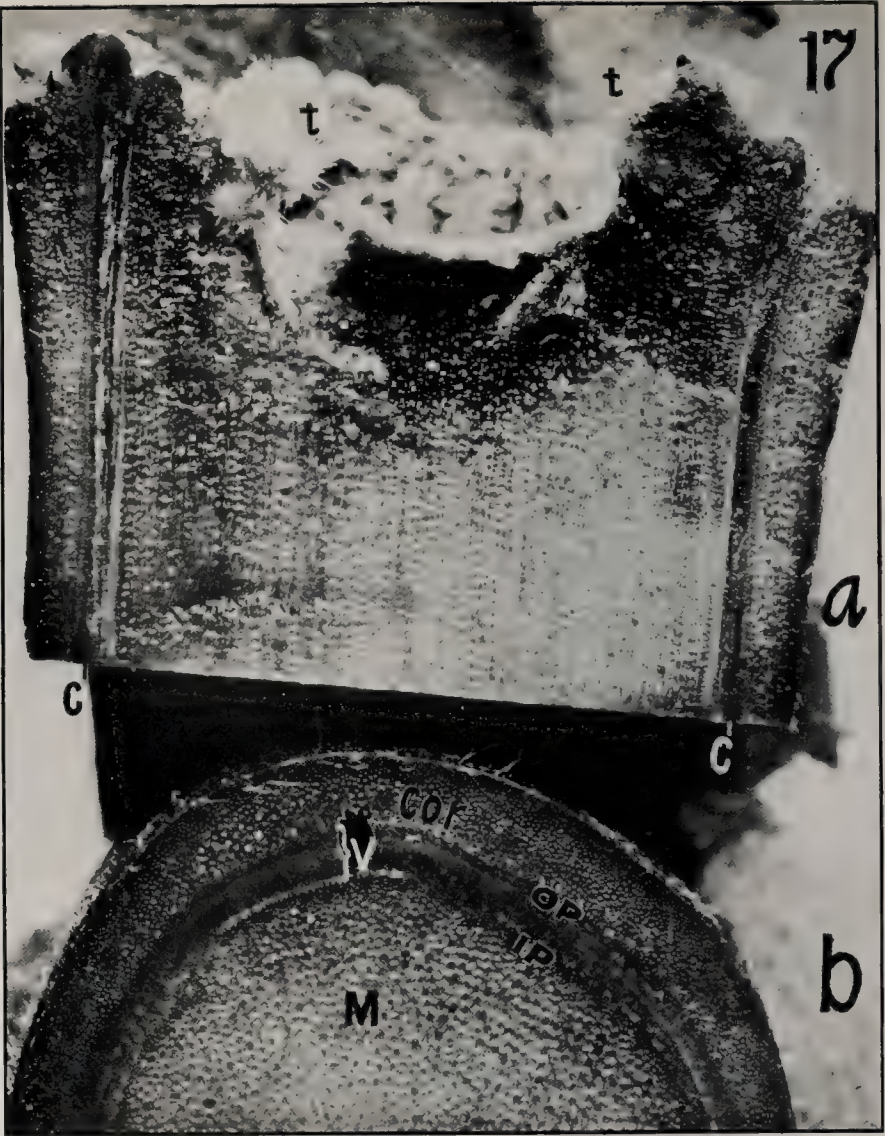
FIG. 76.—Leaf axil crown-gall teratoids on the garden nasturtium (*Tropæolum*). Plants inoculated August 5, 1916 (hop strain through sunflower in 1915, colony 1). The tumors developed both leafy shoots (X) and roots (Y, Z), but they are now decaying. Photo. November 13, 1916. (Nearly natural size.)

FIG. 77.—Leaf axil crown-gall teratoids on cabbage. Inoculated by needle-pricks September 29, 1916, with the hop strain of *Bact. tumefaciens*. The inner edge of the left tumor is smooth (membranous) and bears a leafy shoot. The rest of this tumor, and the whole of the right tumor, is naked and sarcomatous. Leaf scars are visible on the stem. Photo. January 4, 1917. ($\times 1\frac{3}{4}$ circa.)



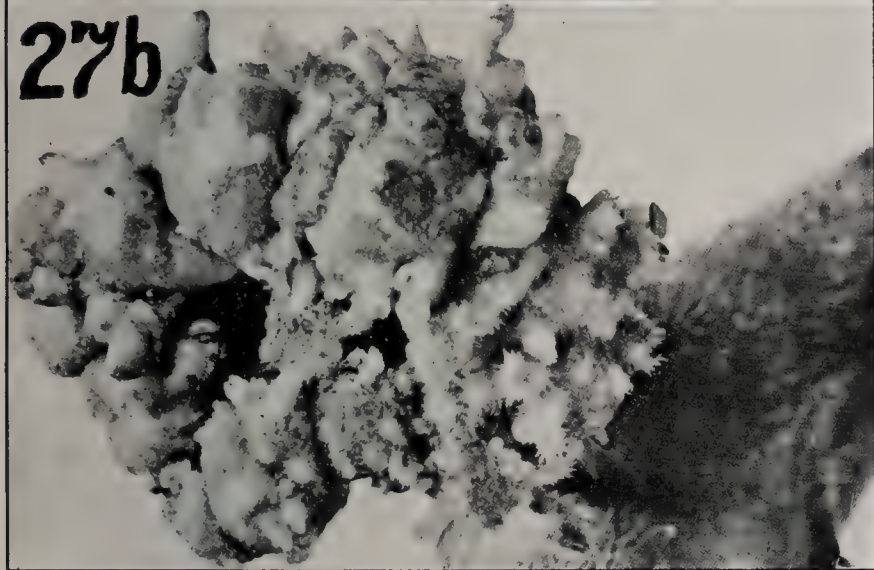


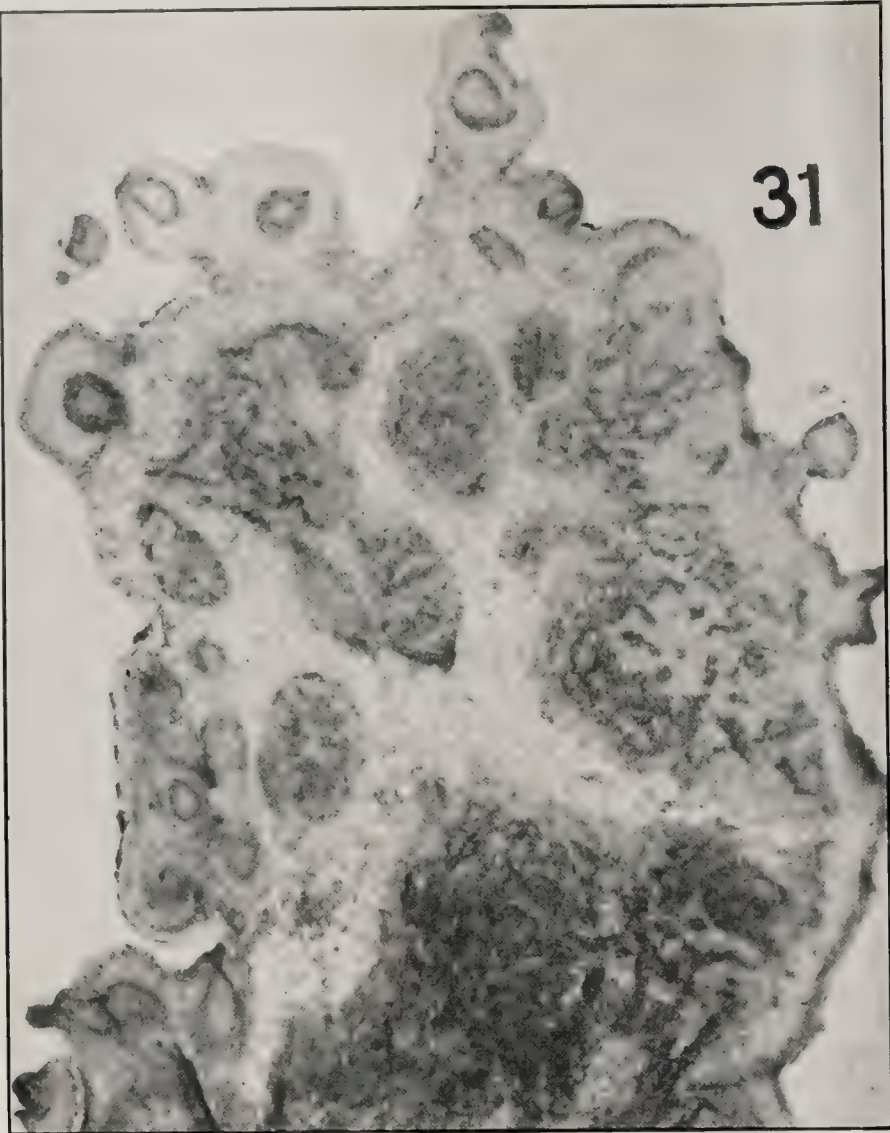


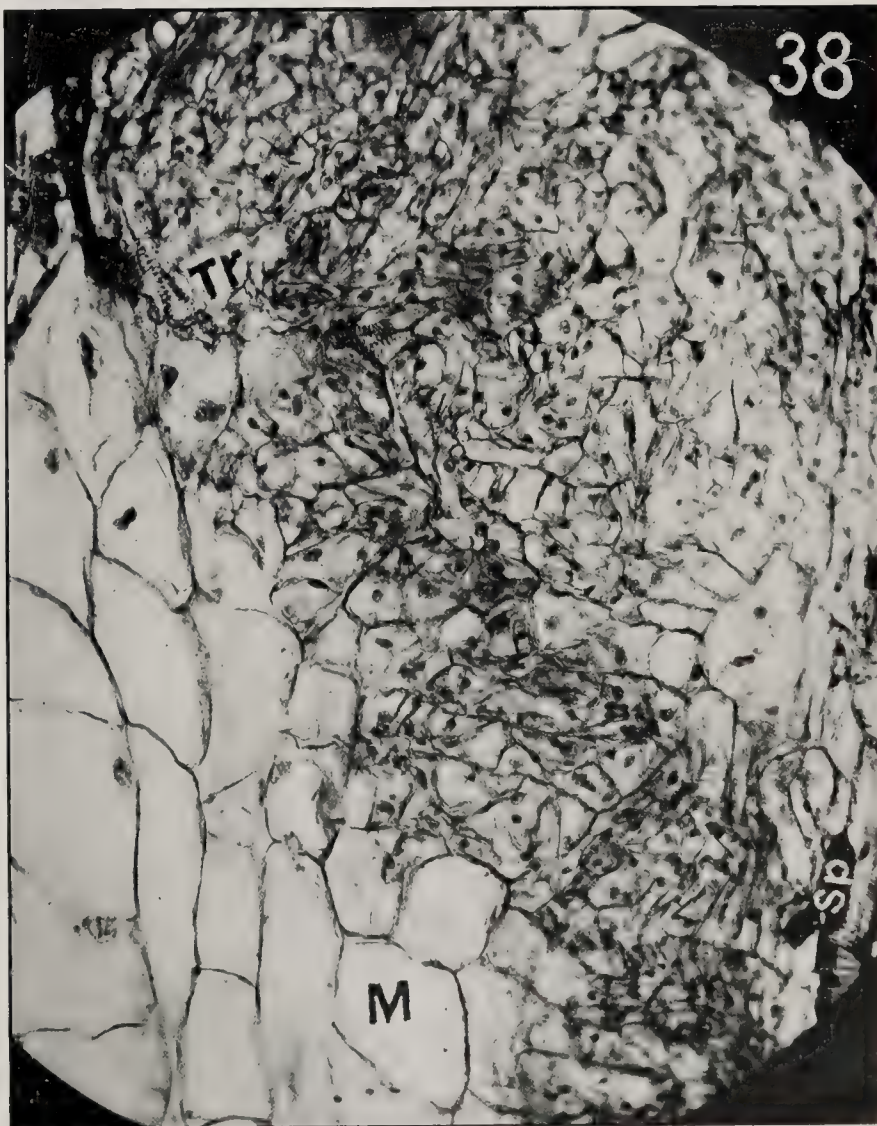
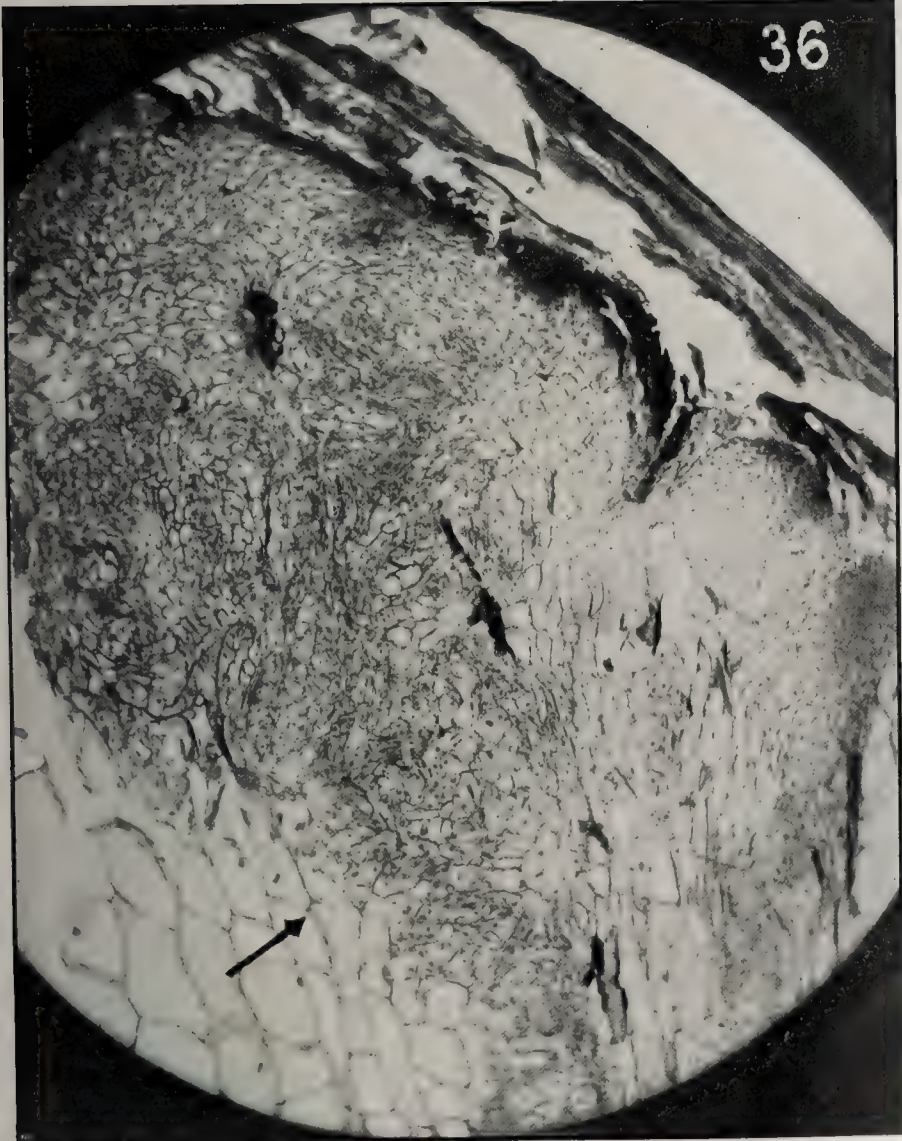
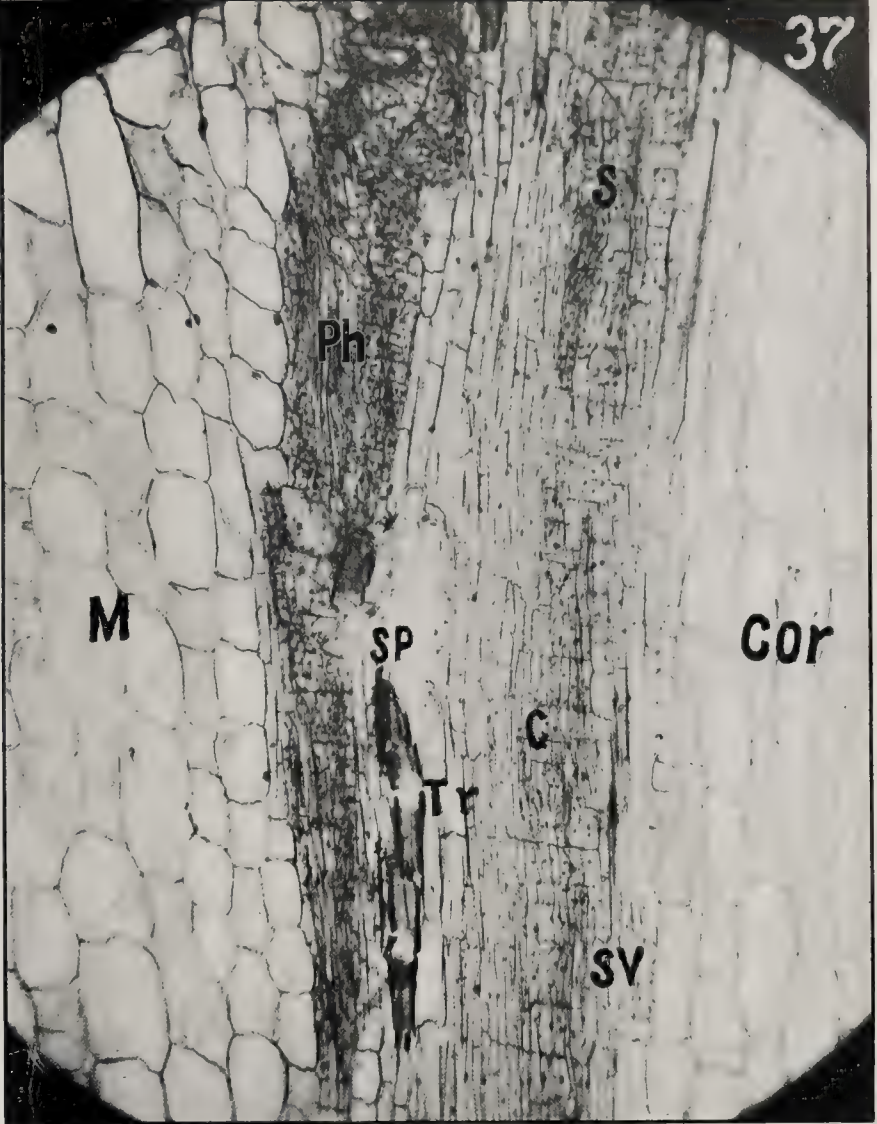
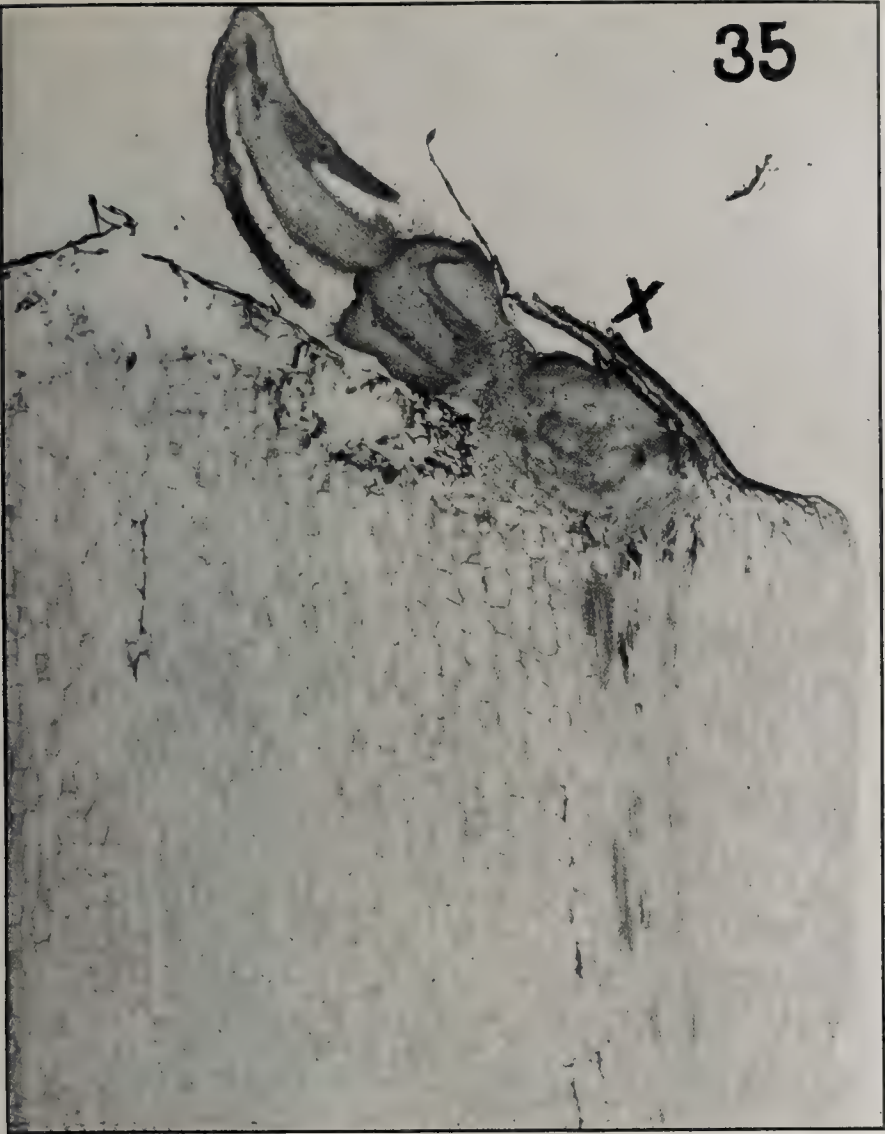


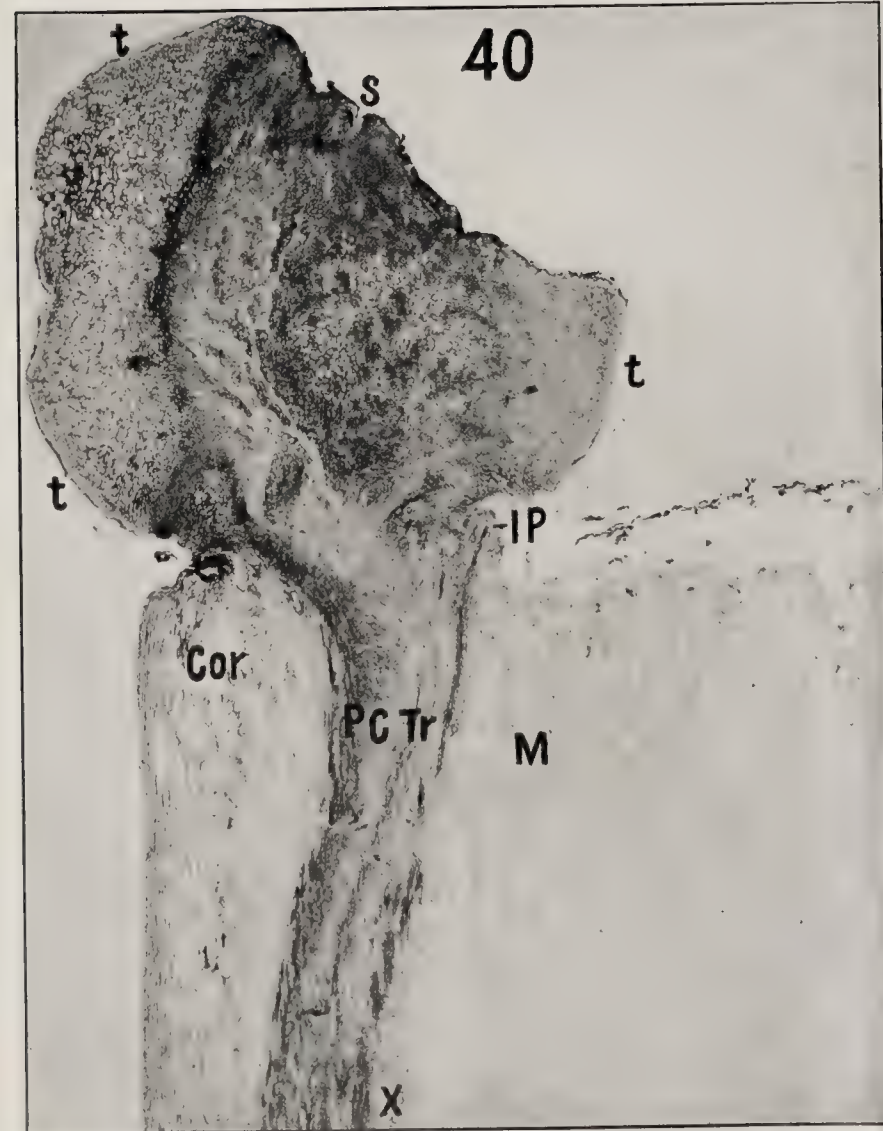
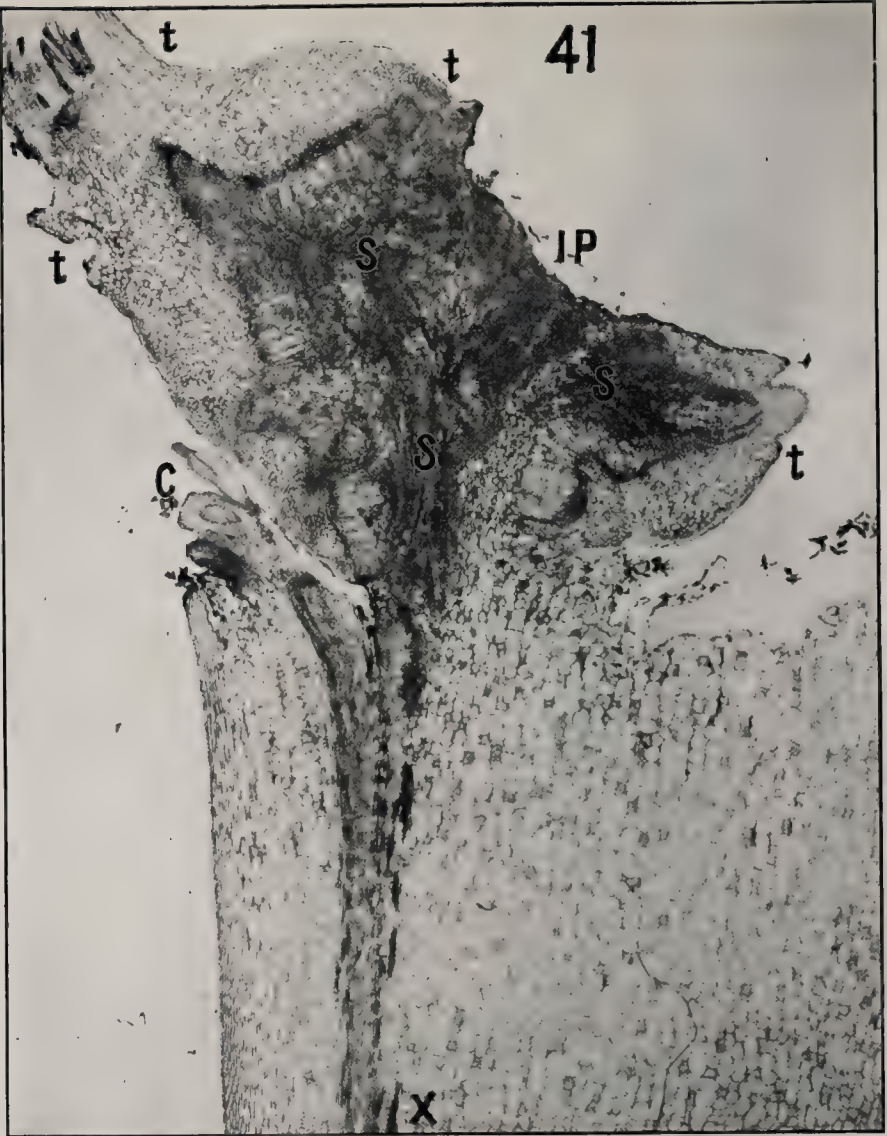


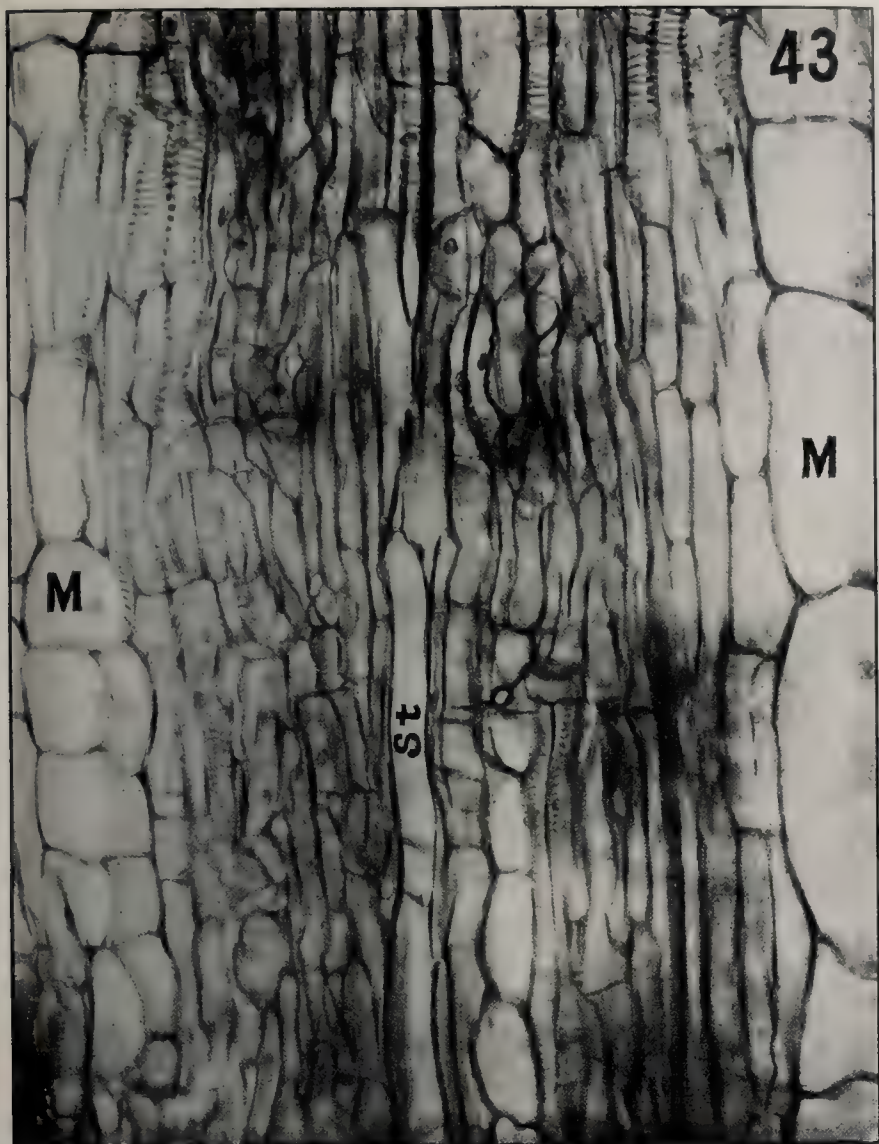


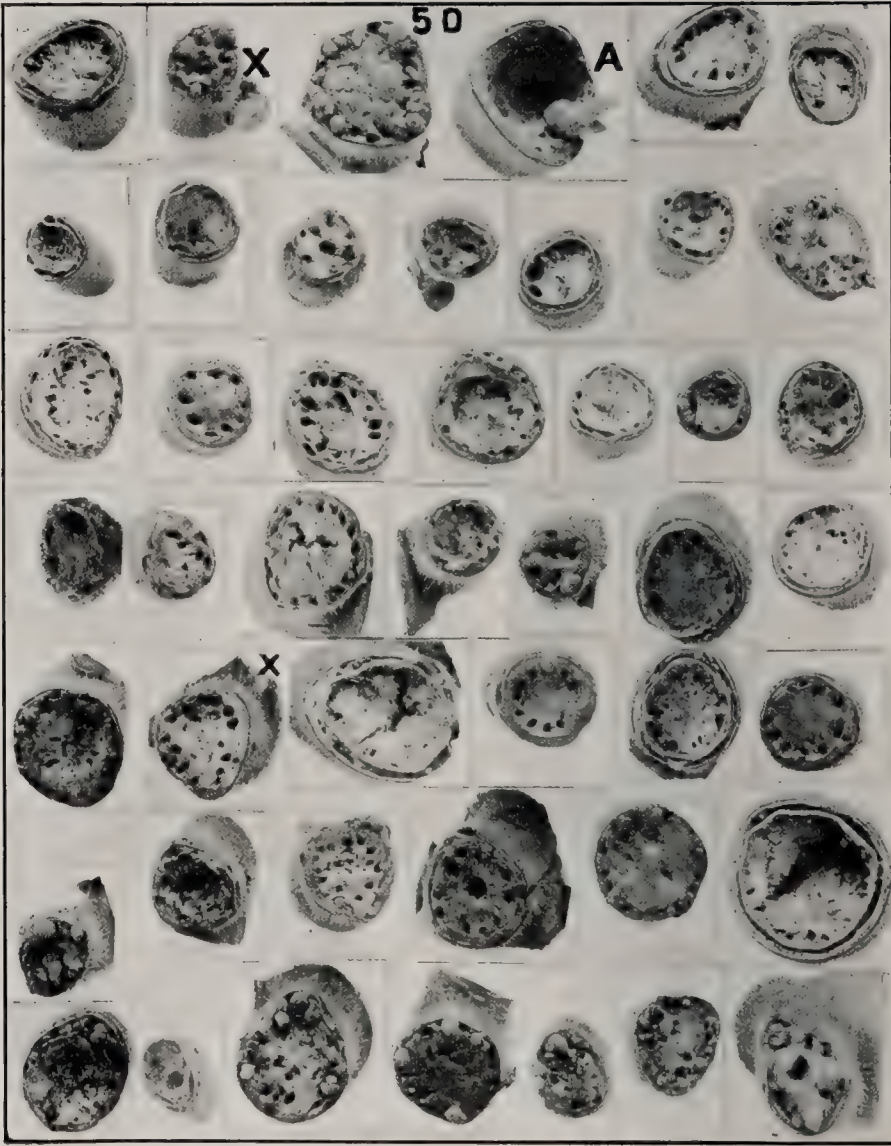
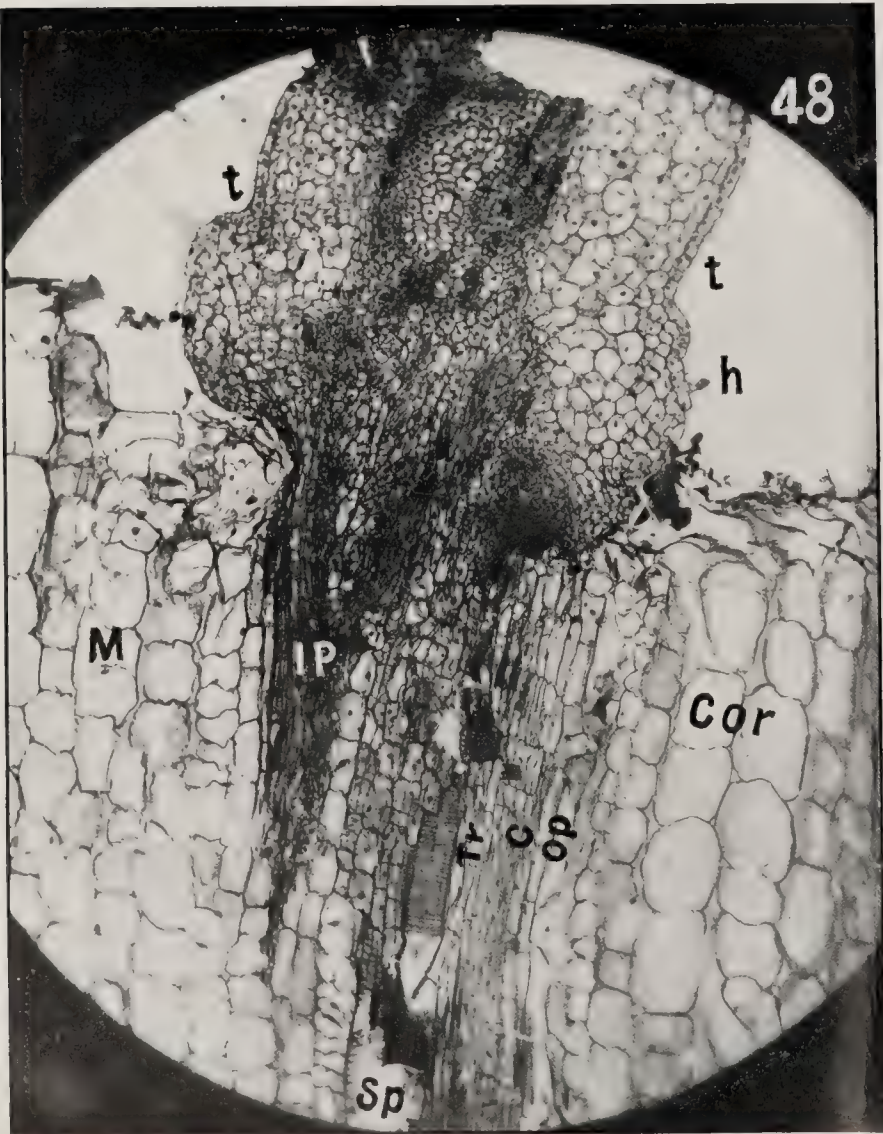








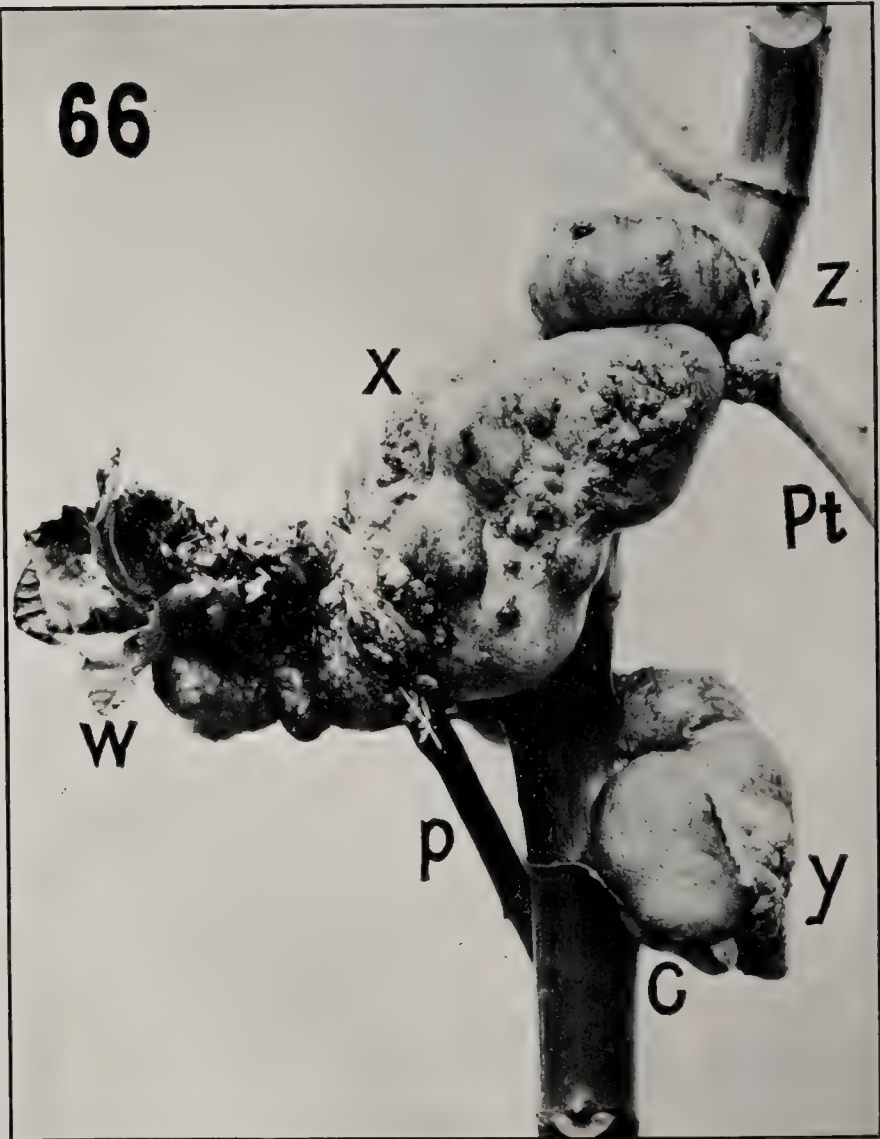


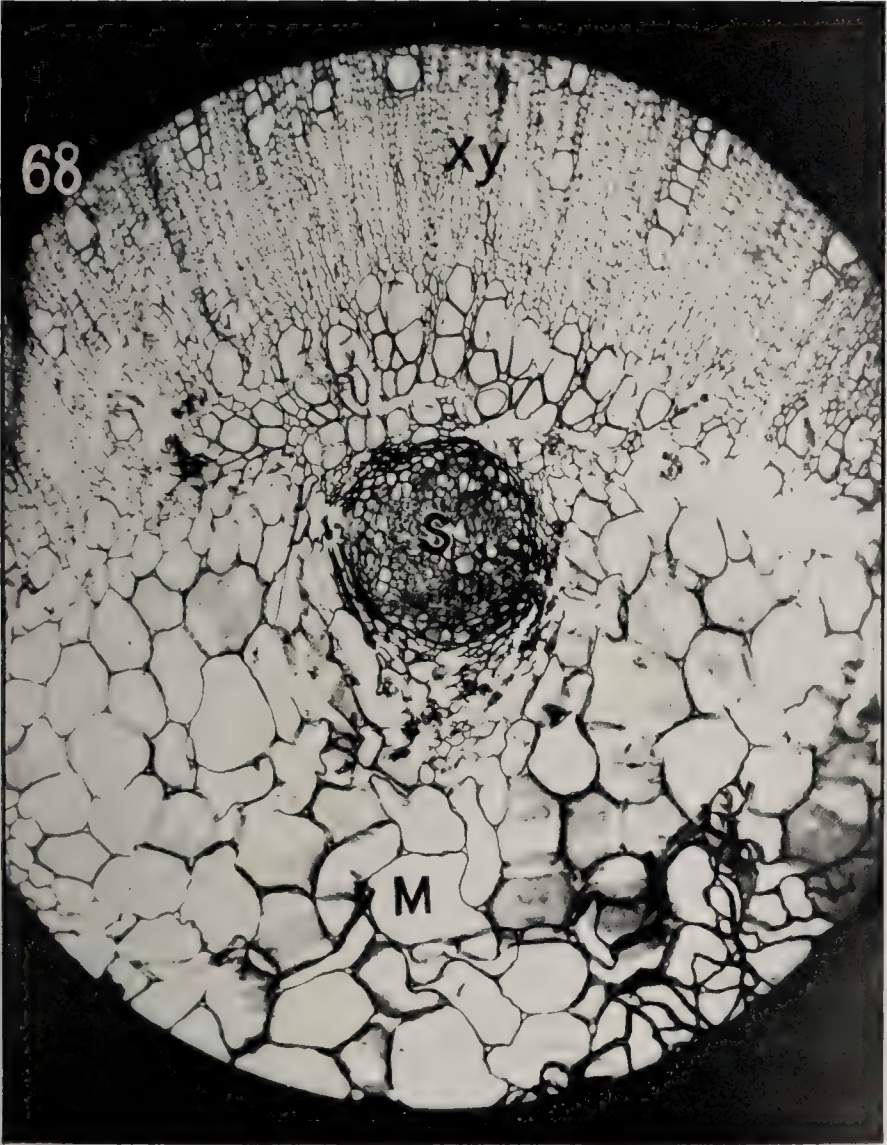
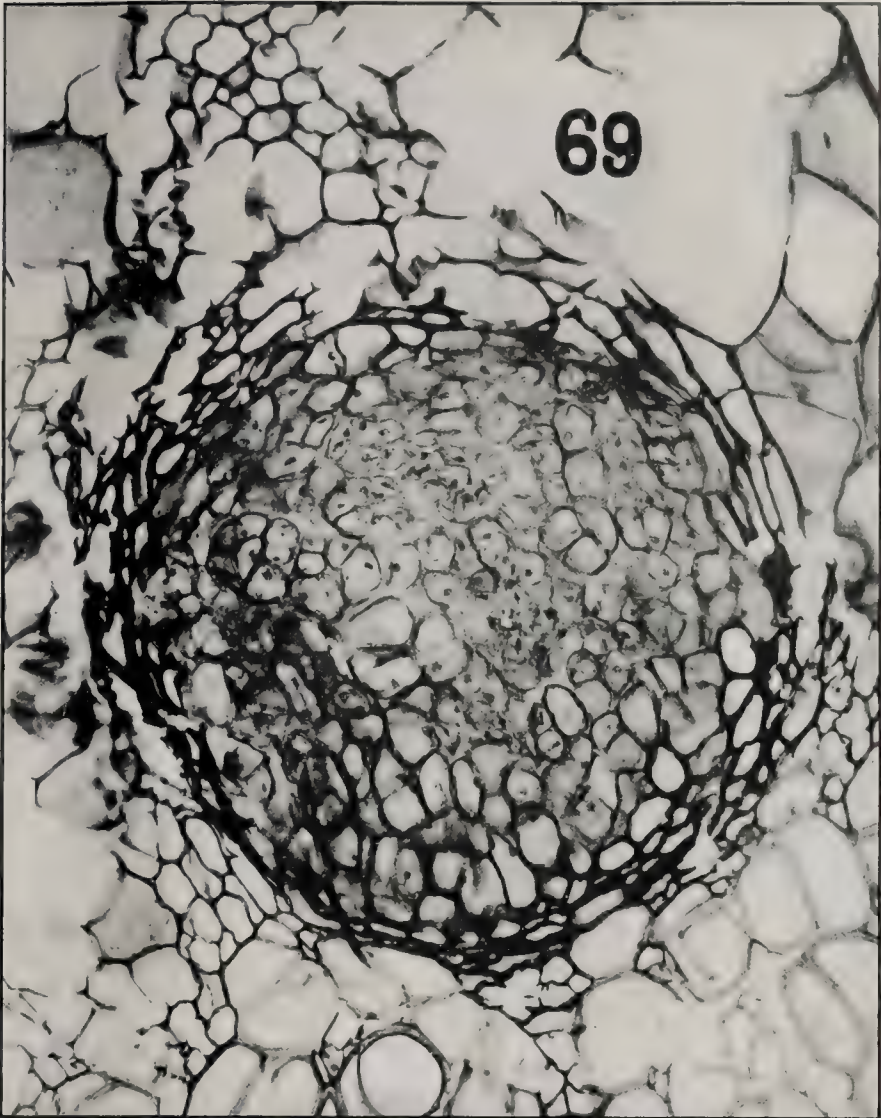


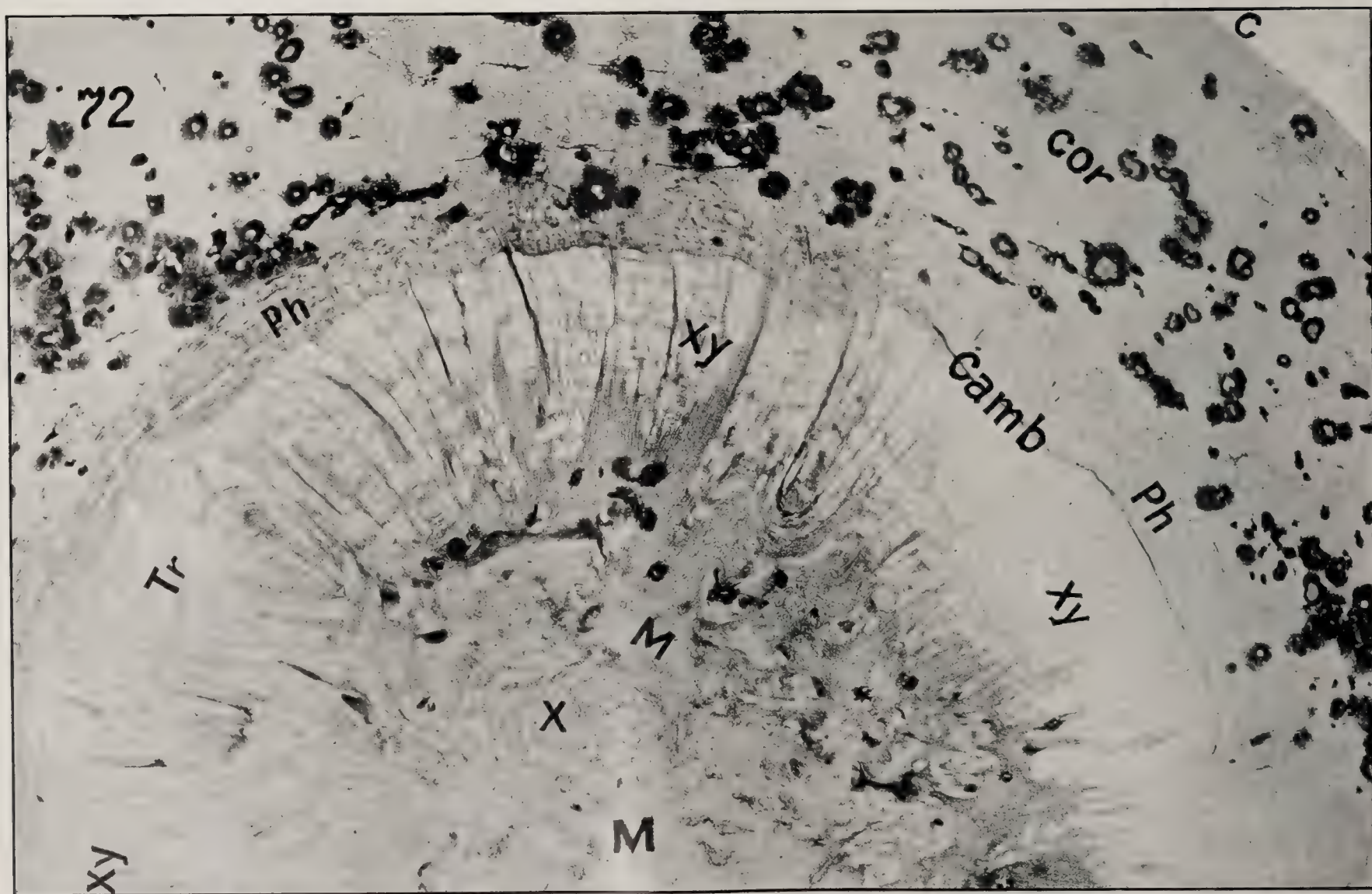
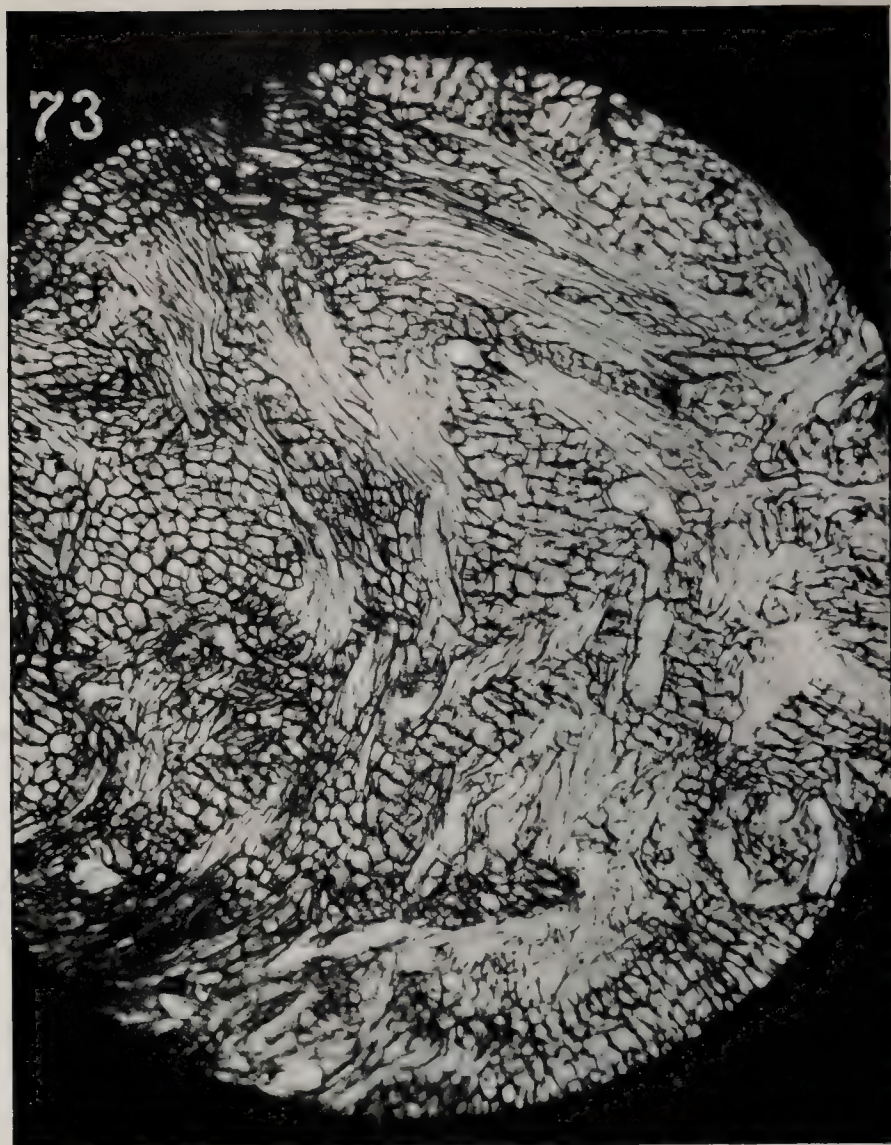




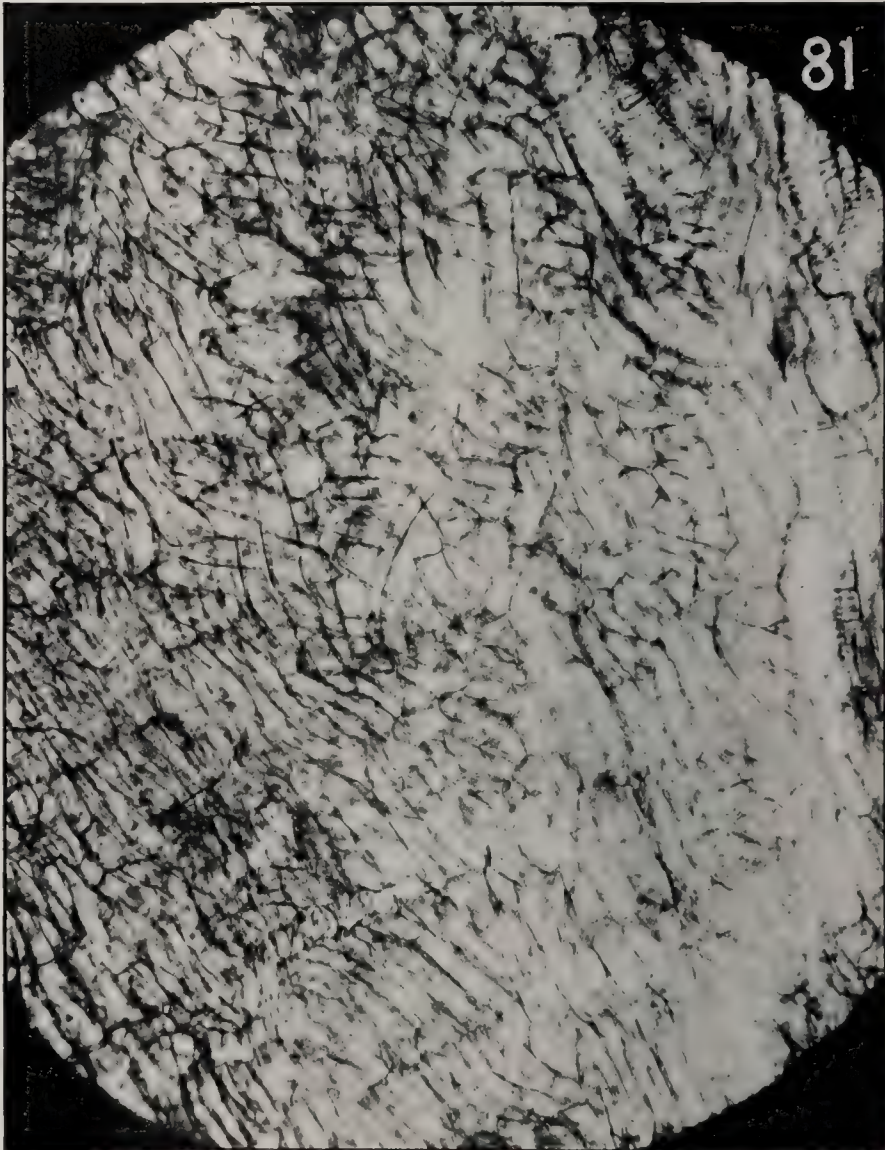
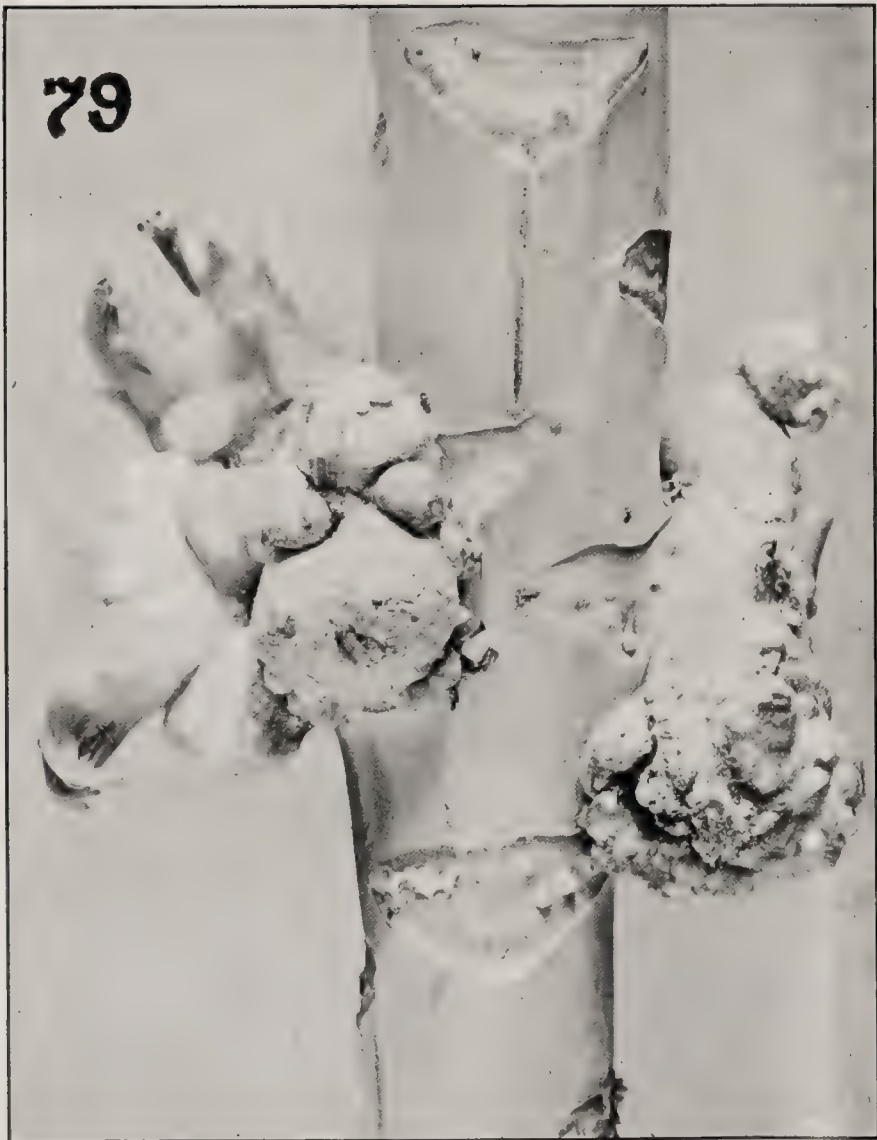


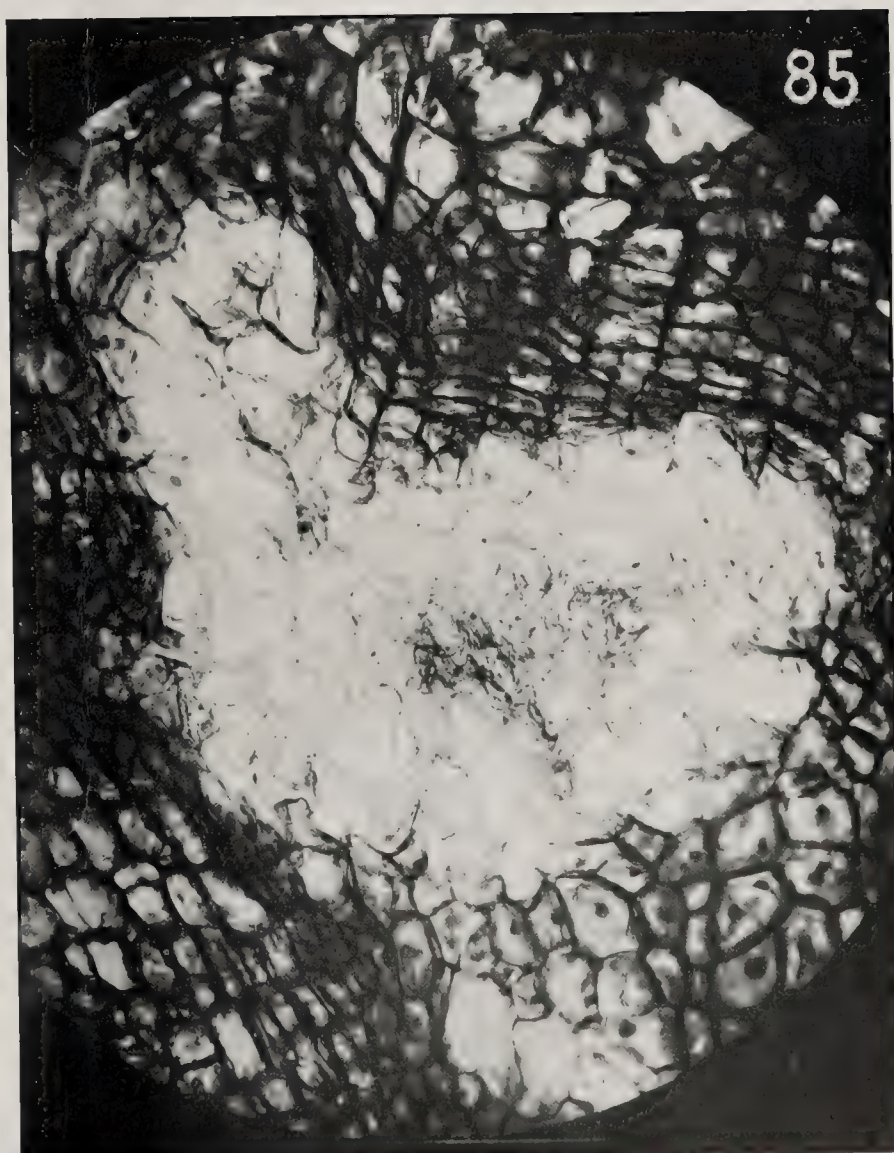
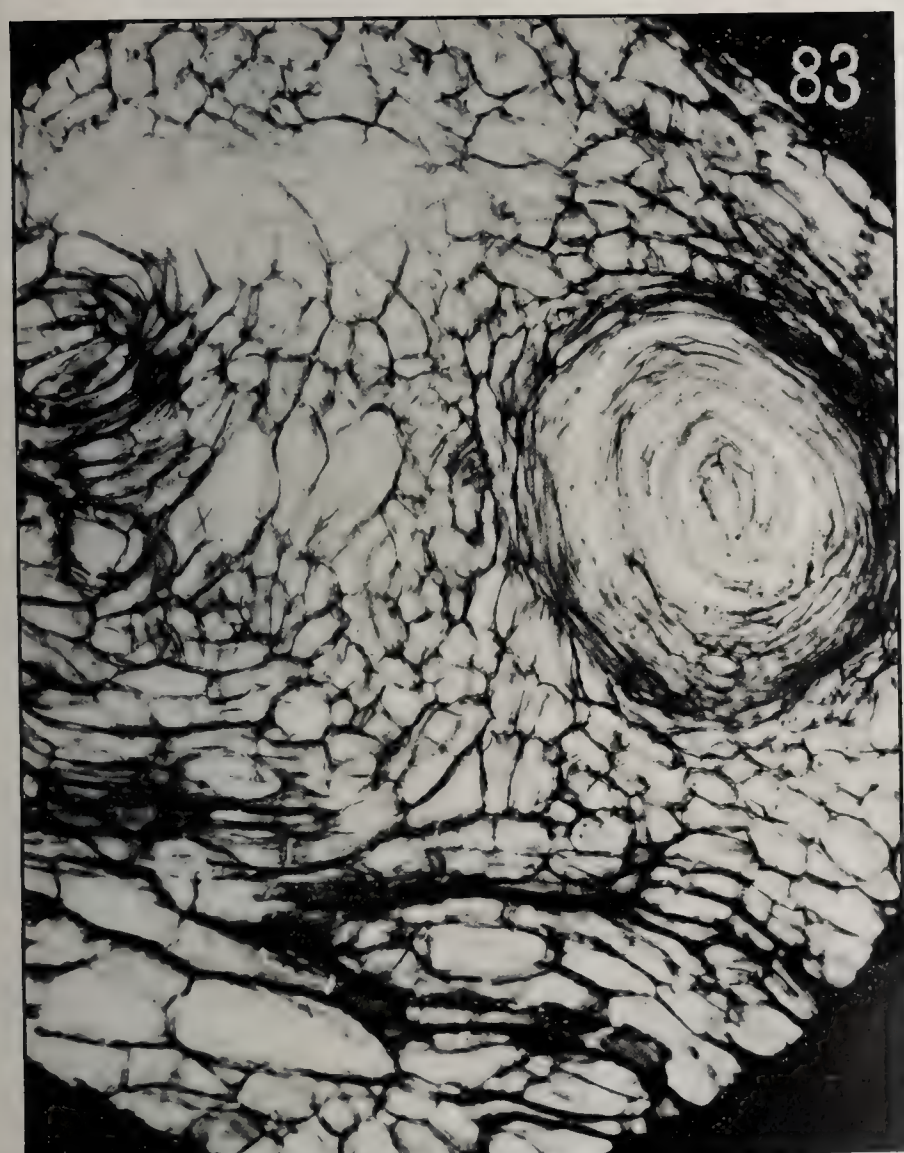
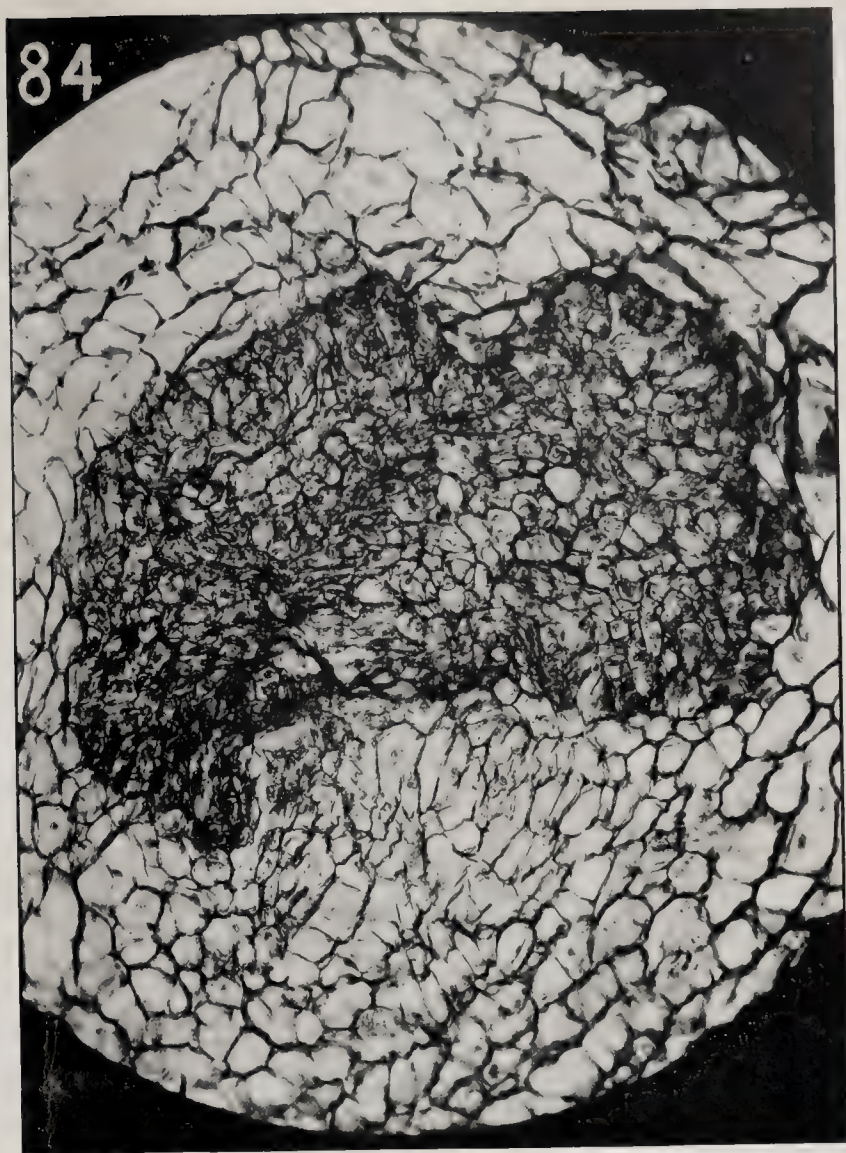
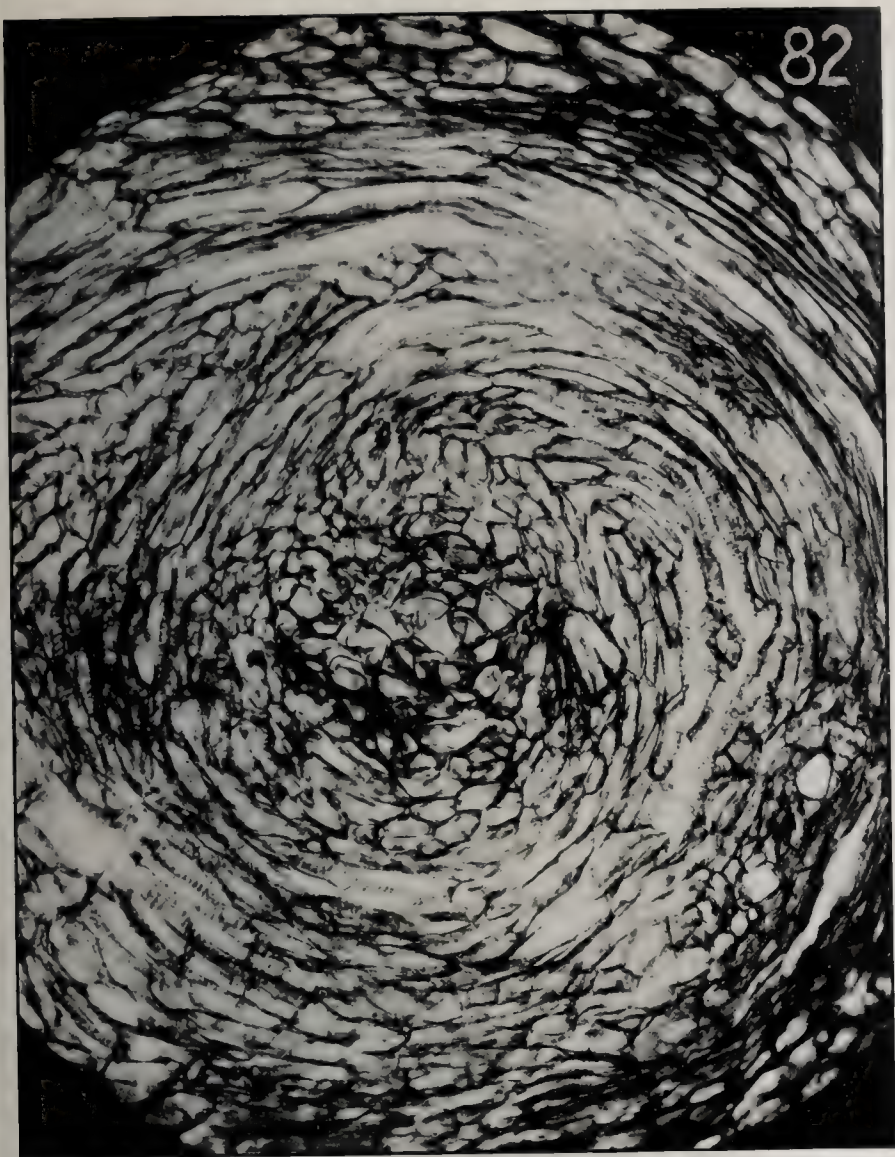


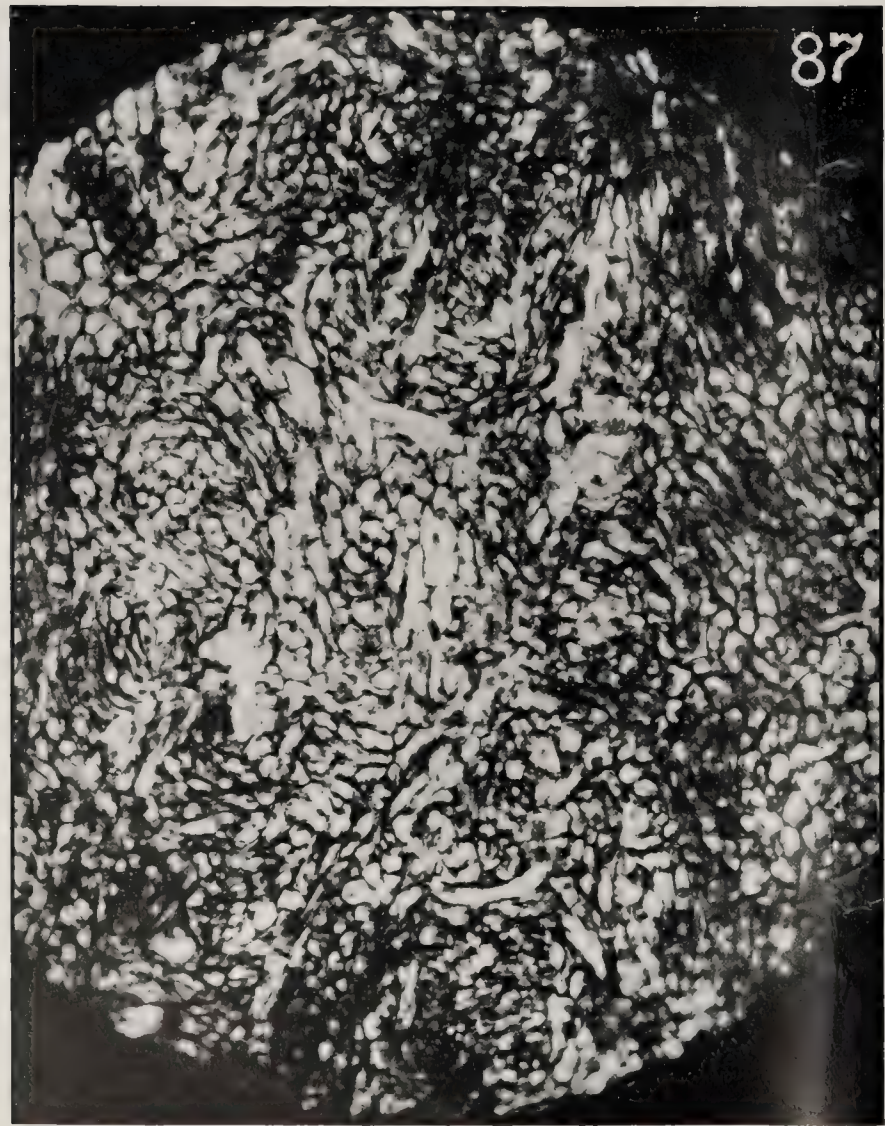
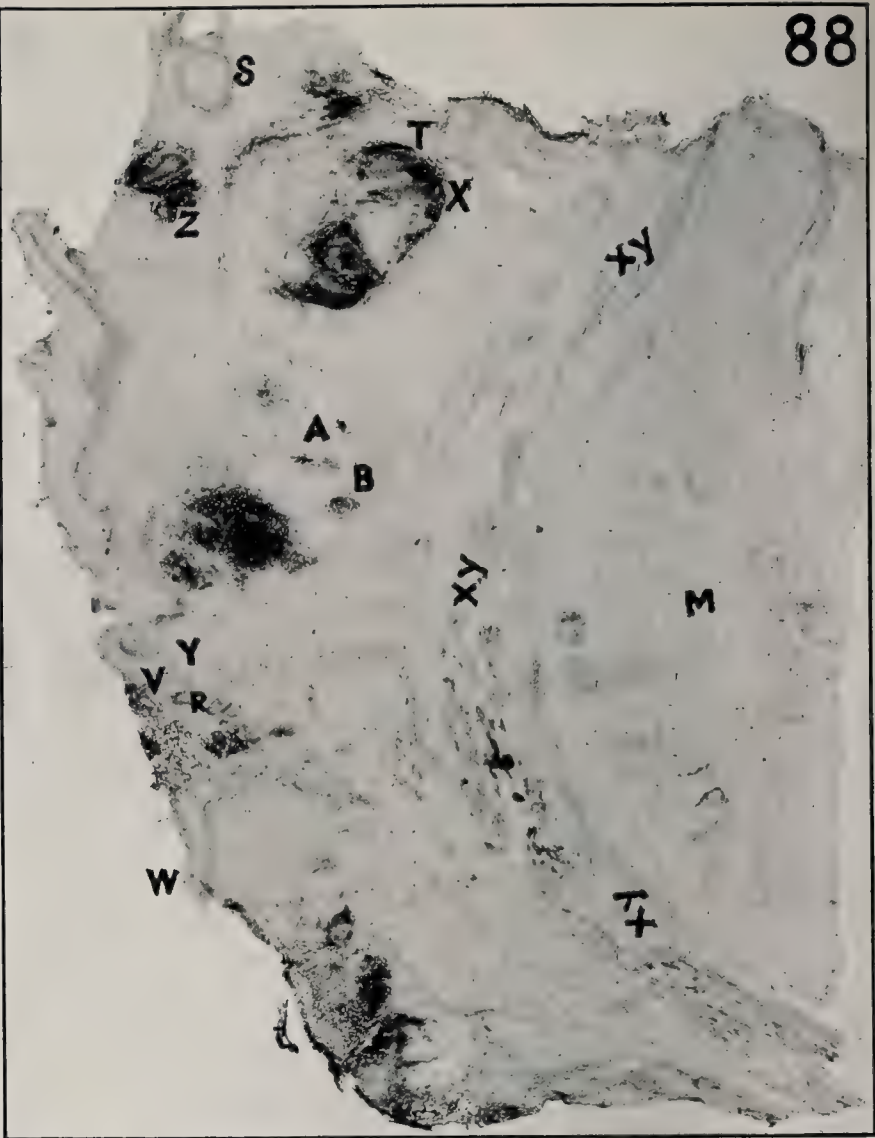


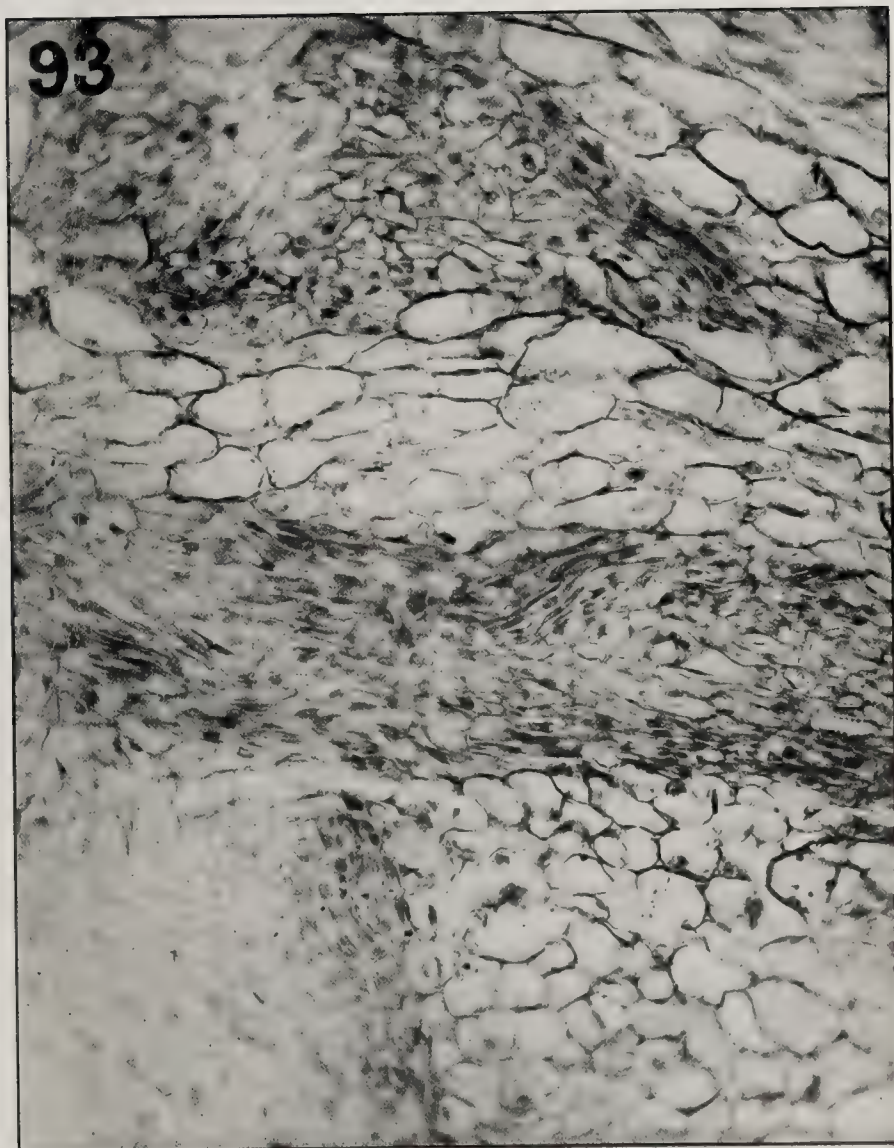
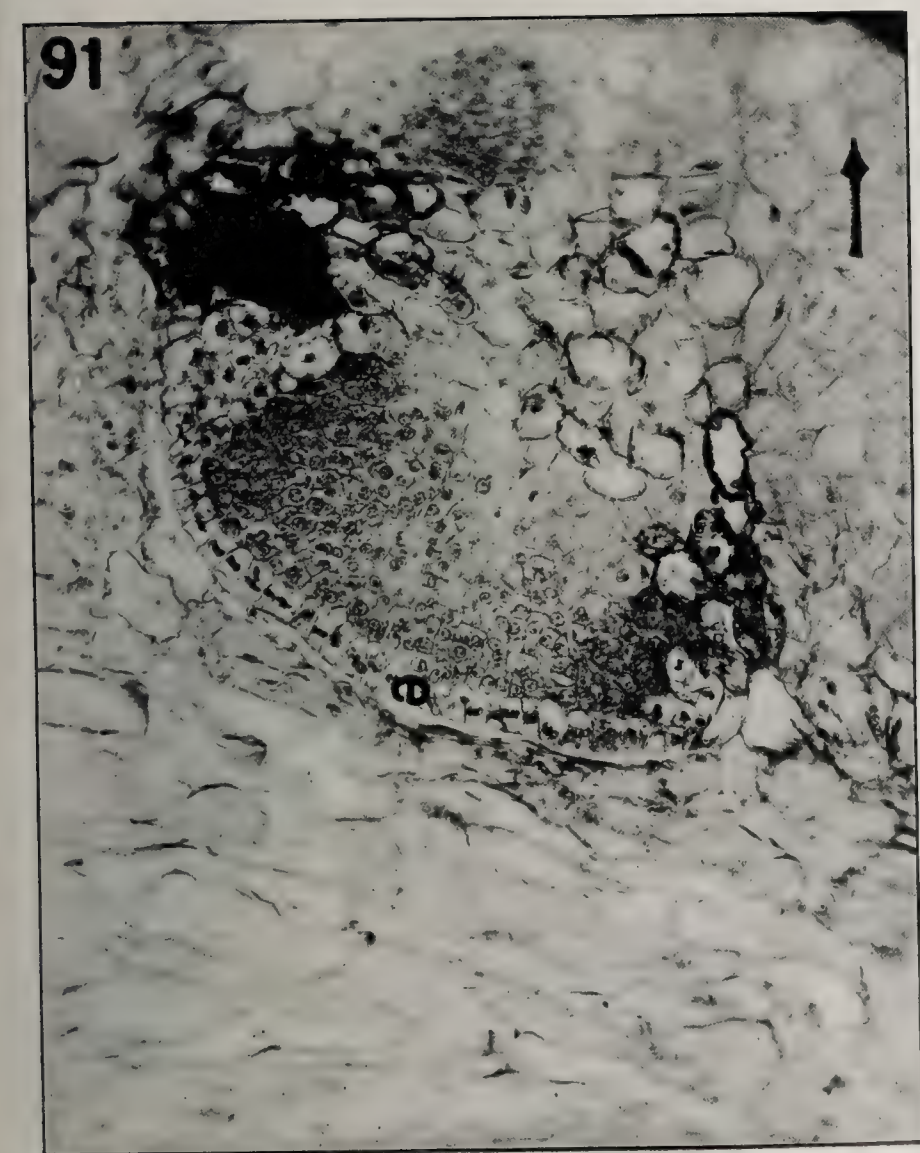
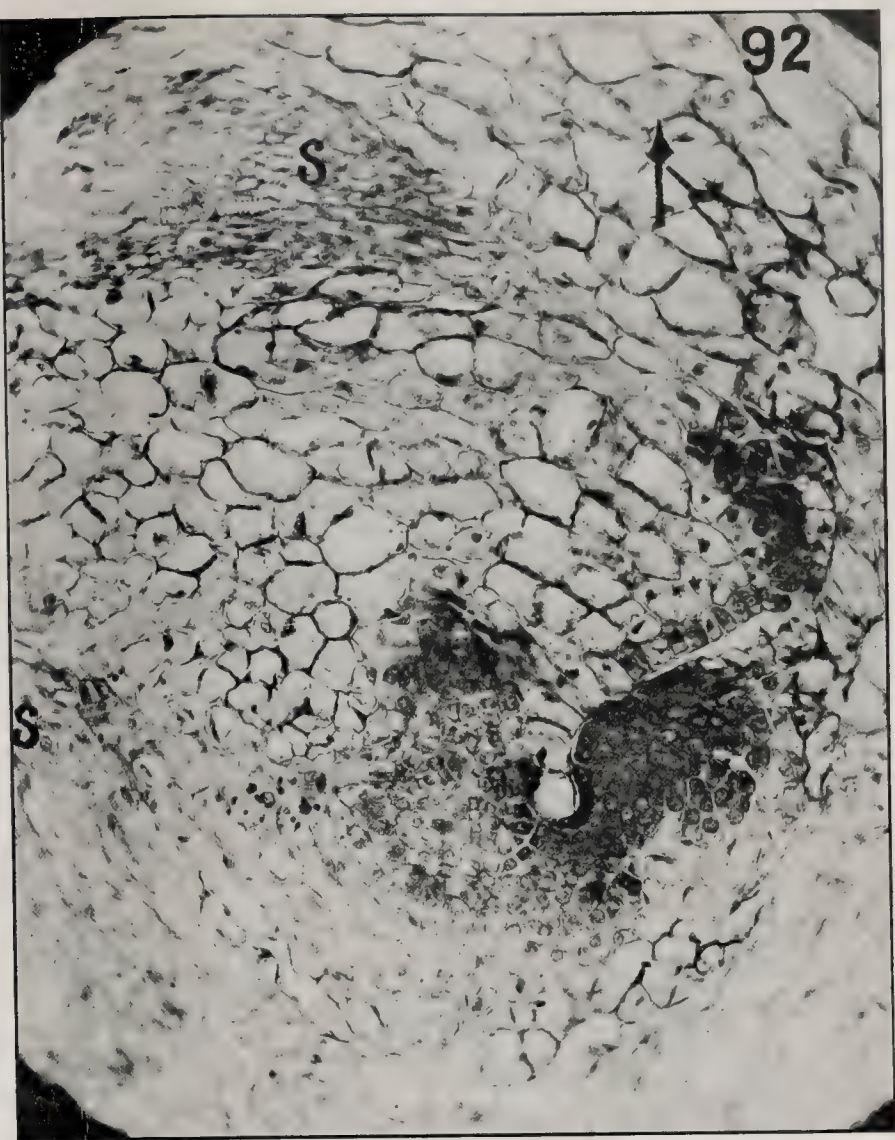
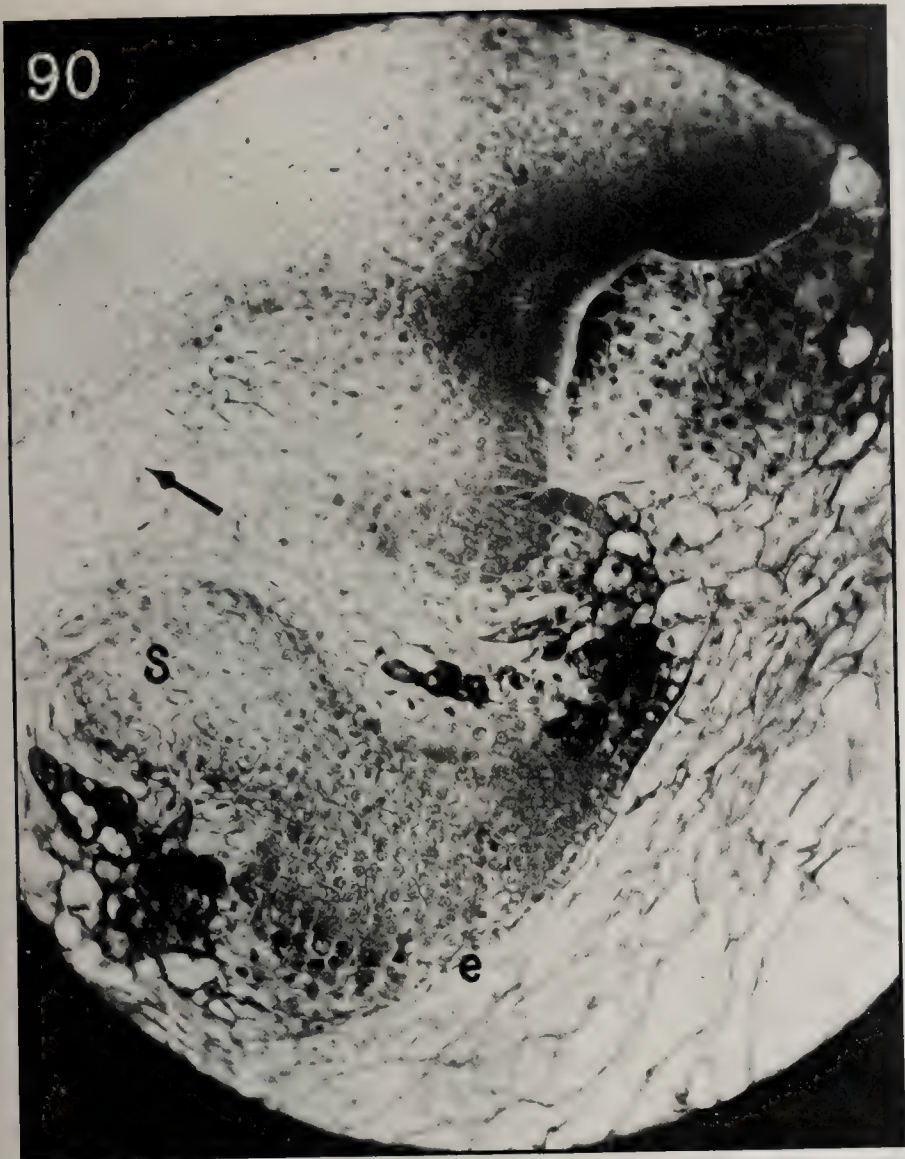


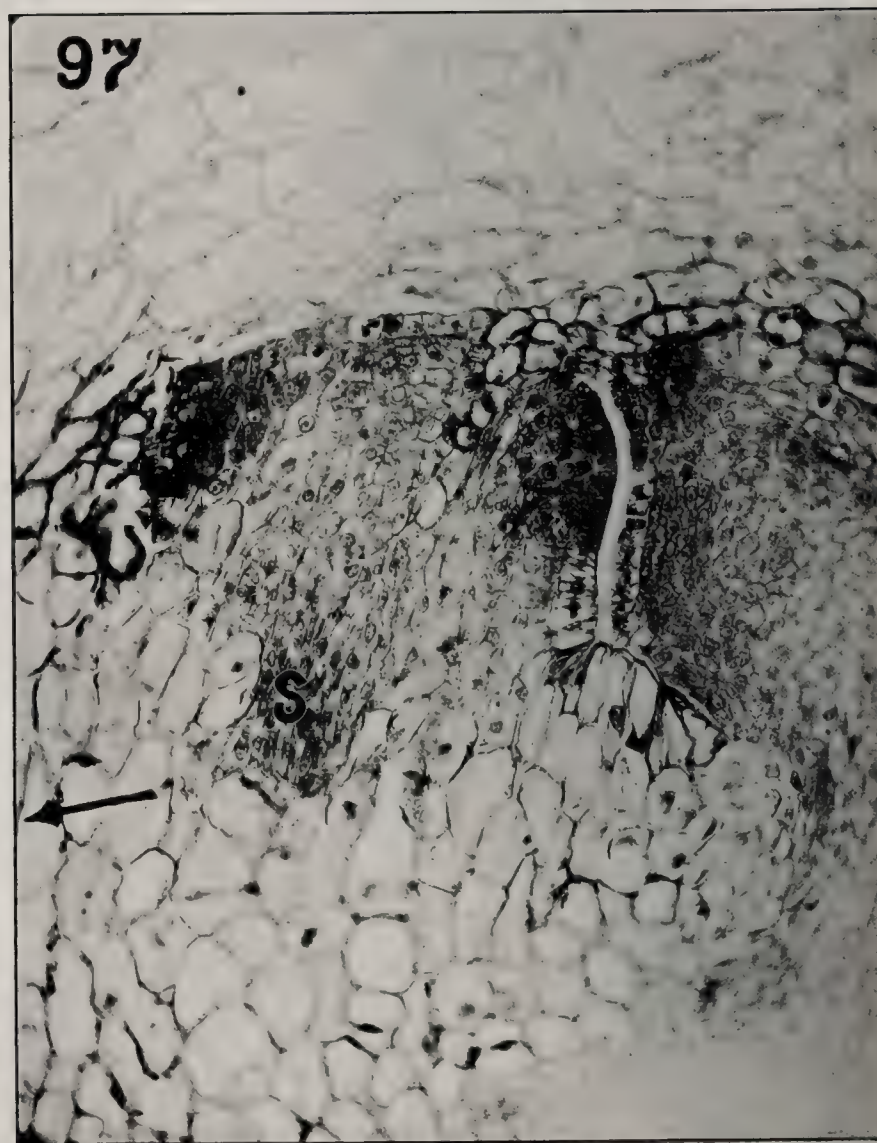
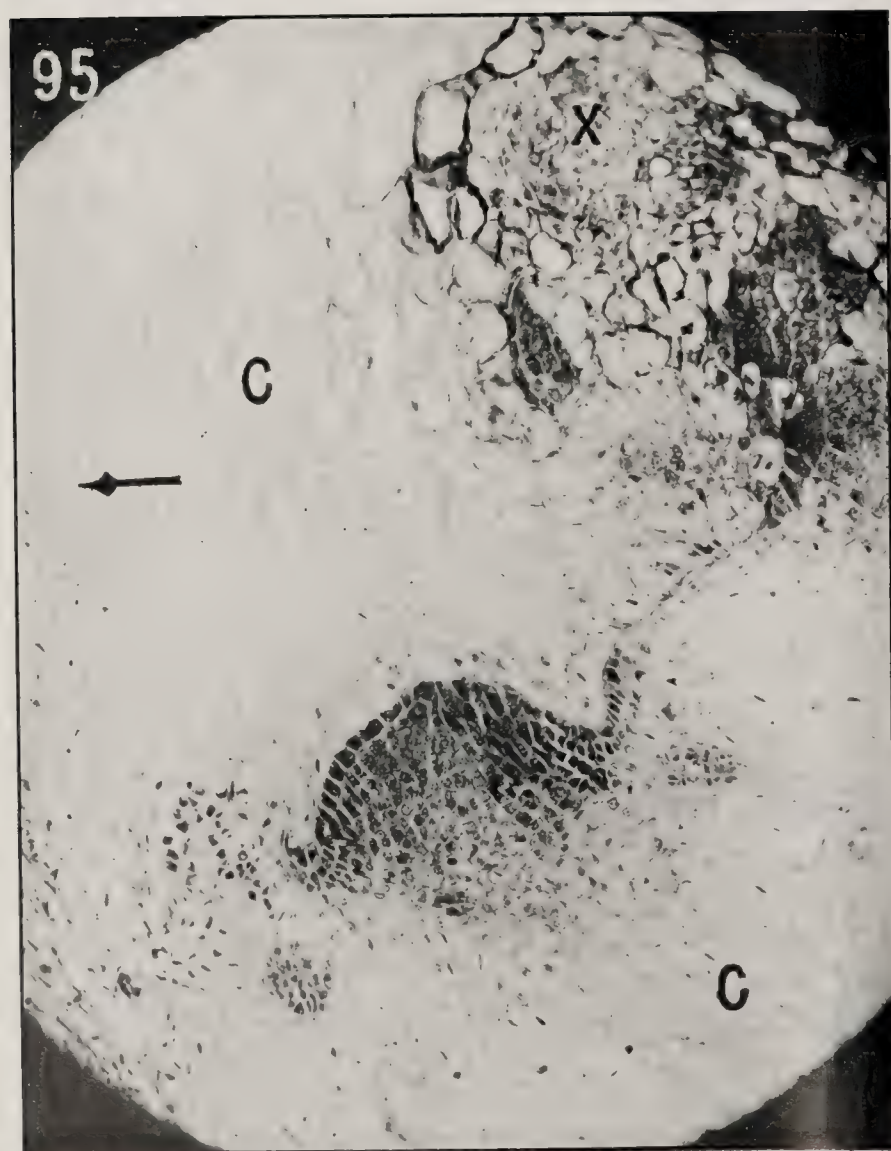
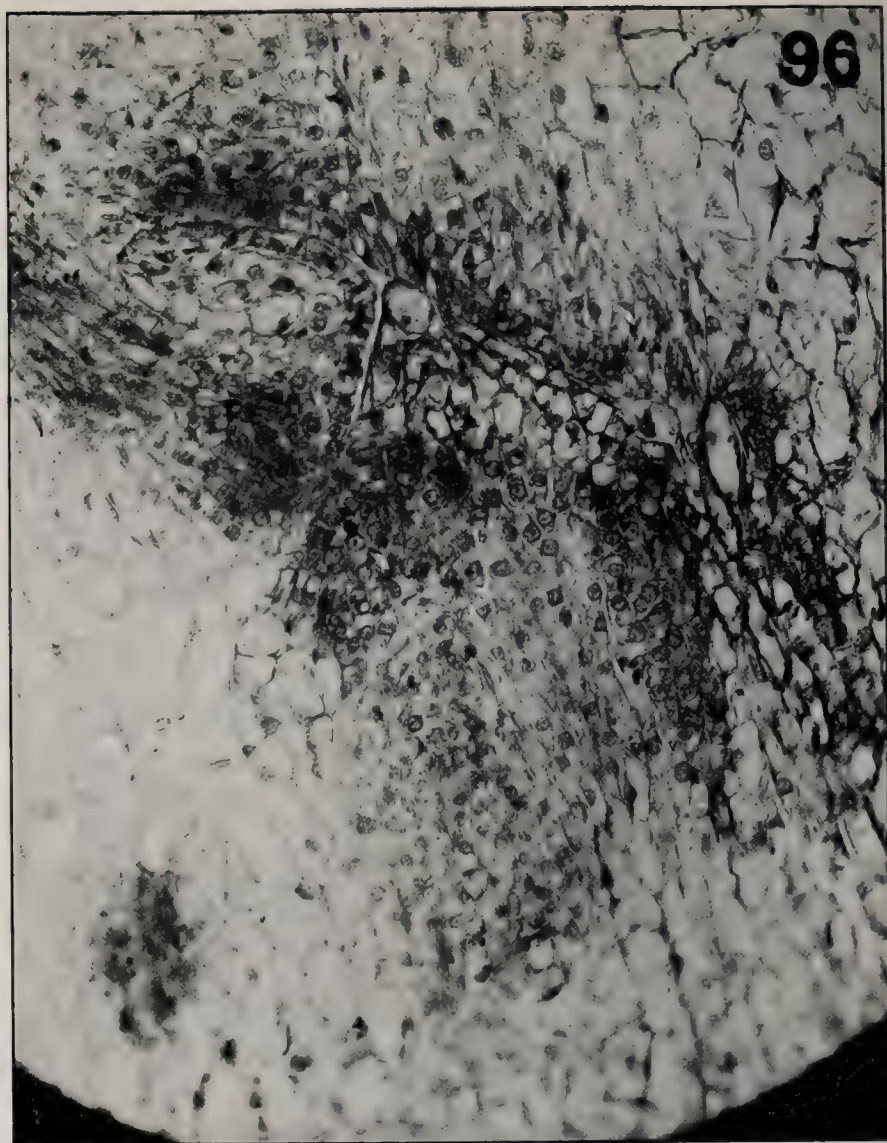
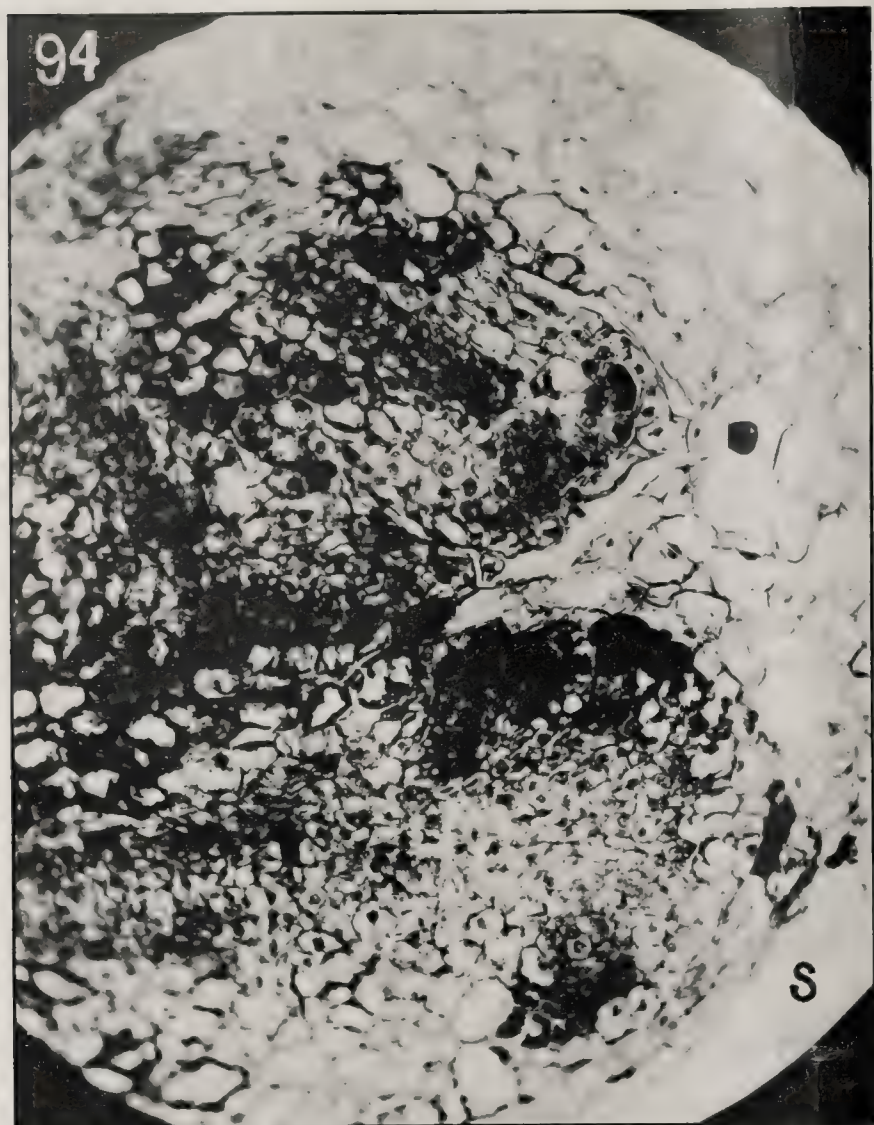


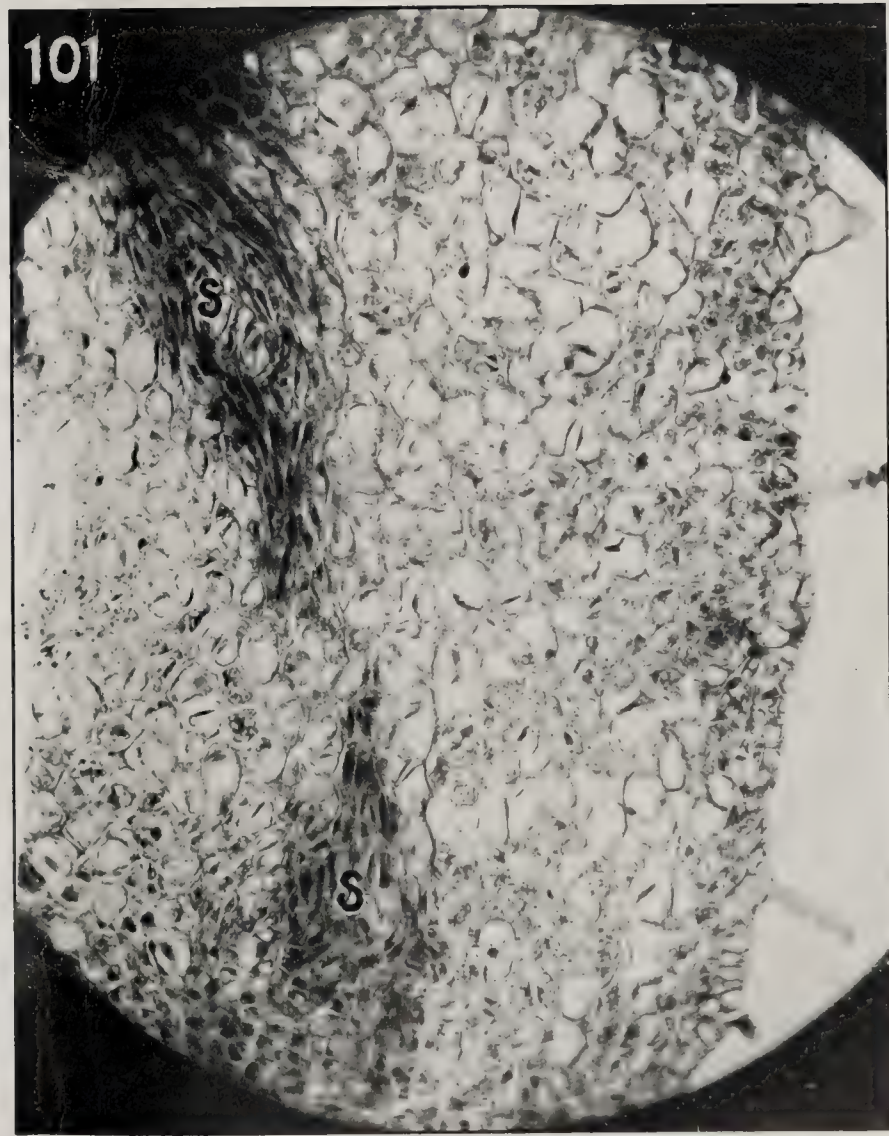
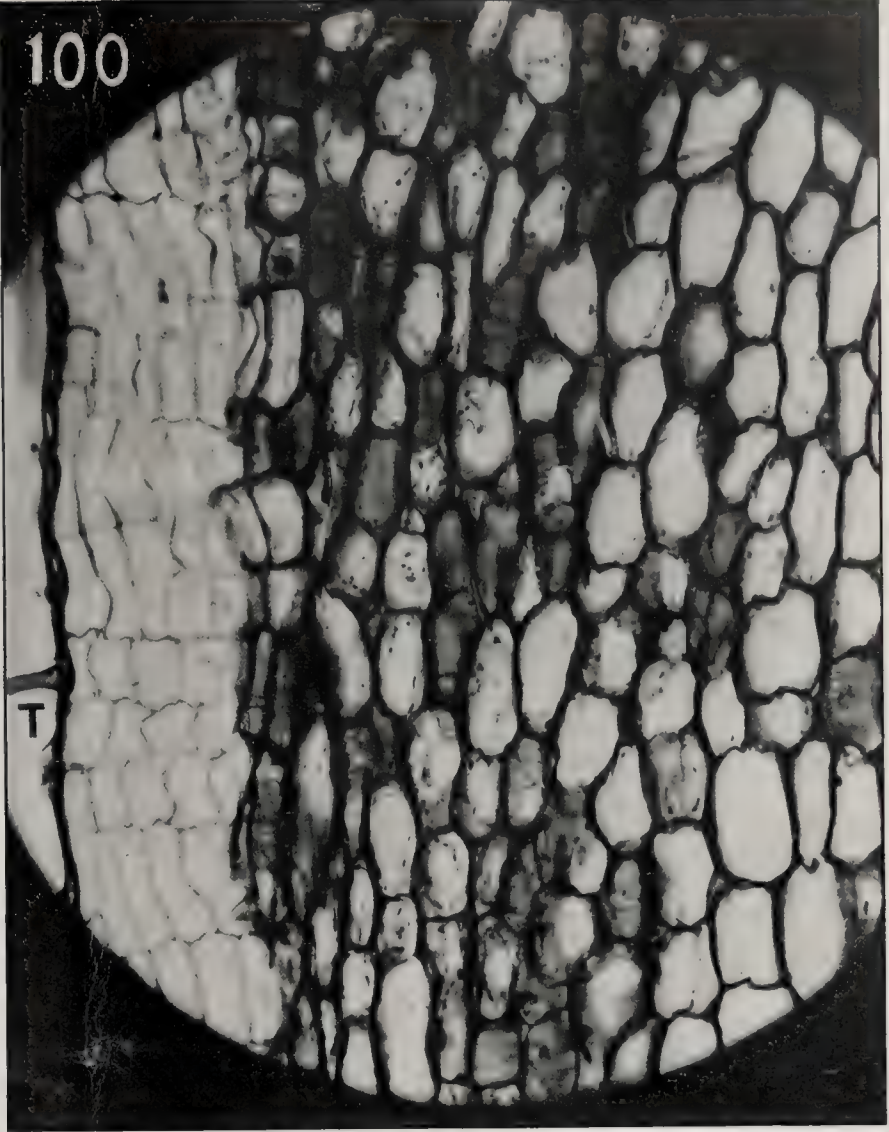
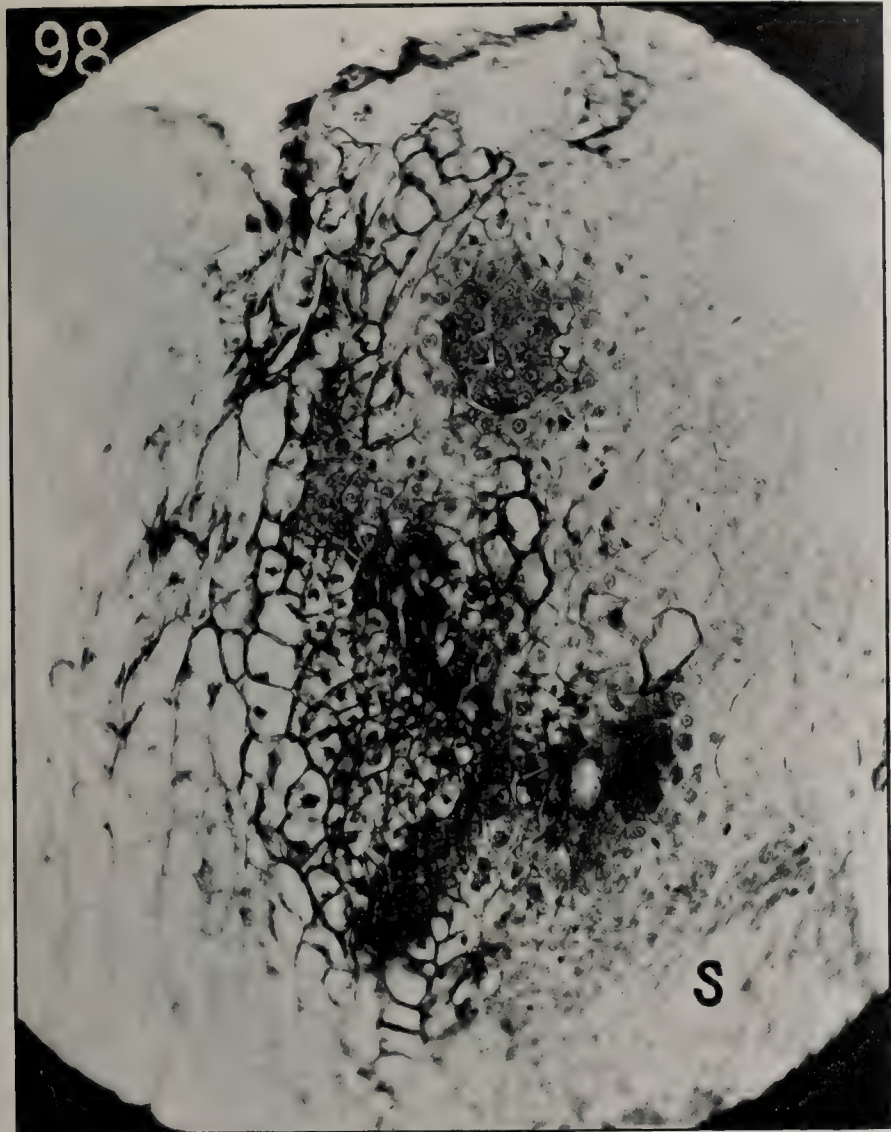


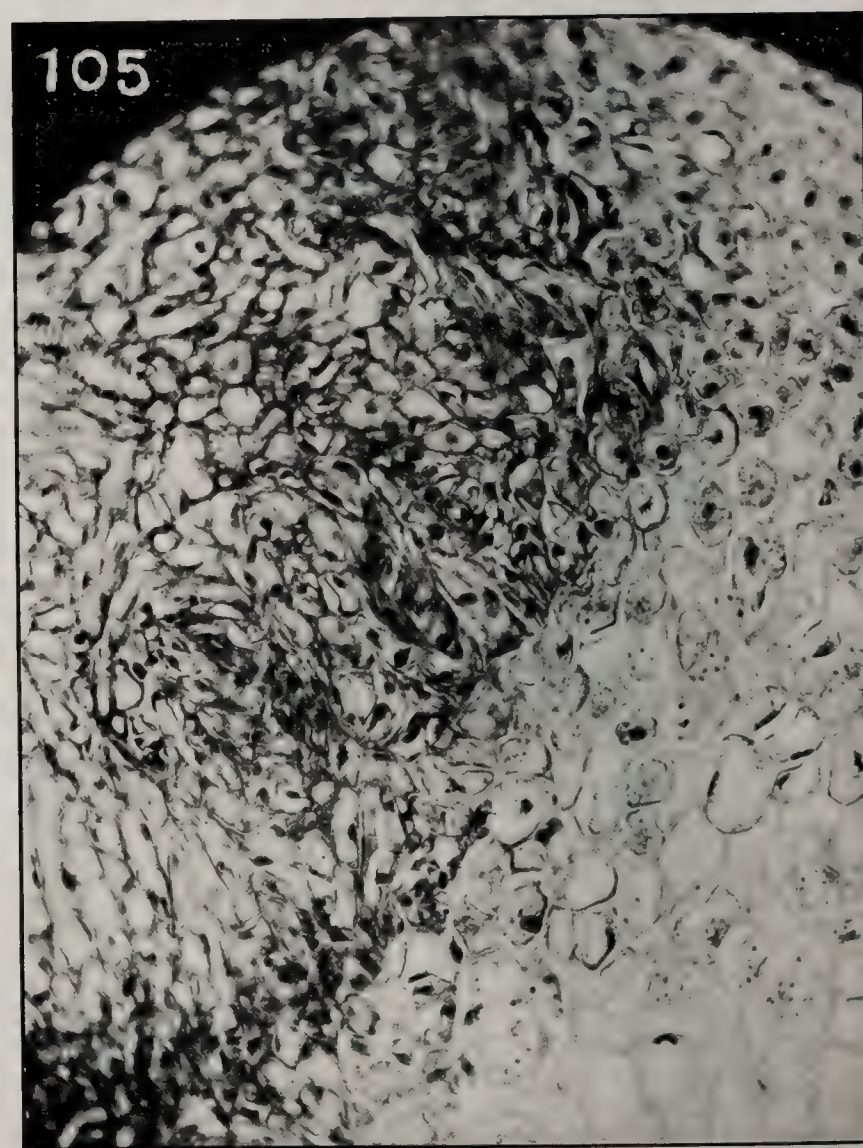
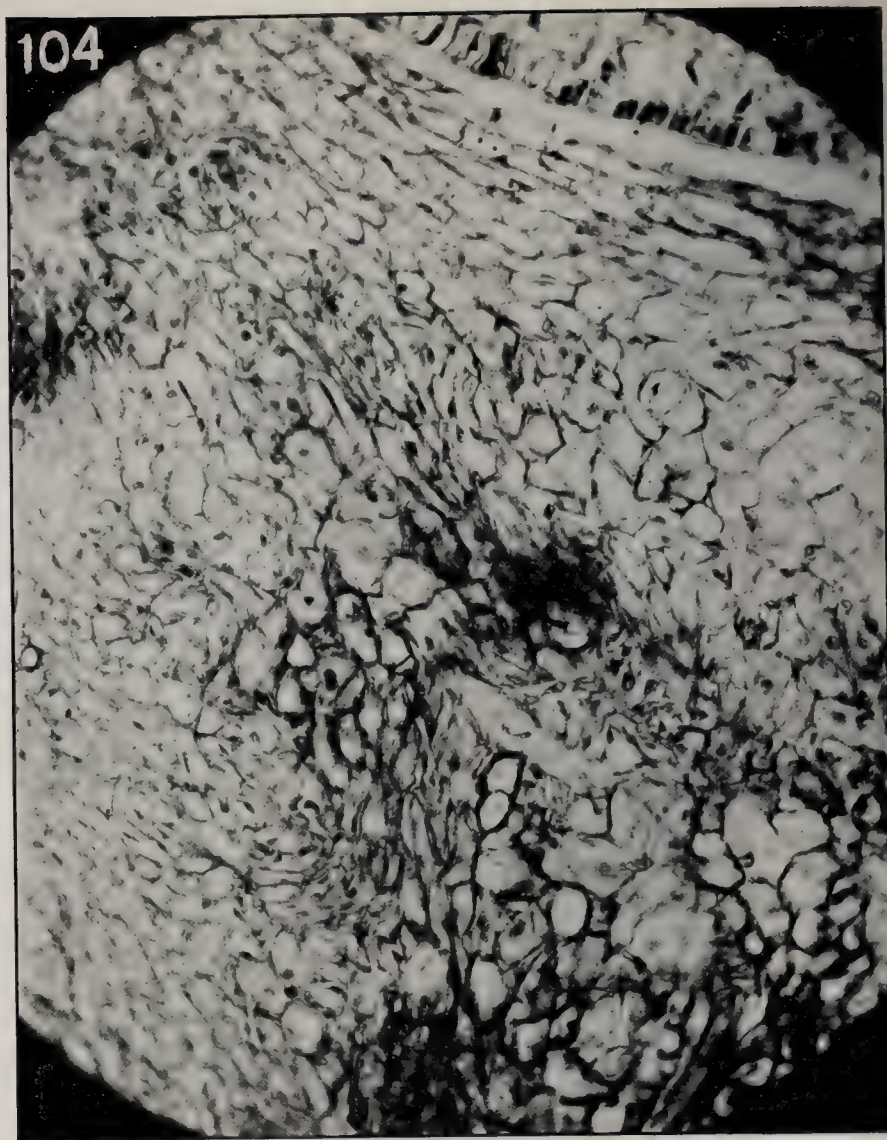
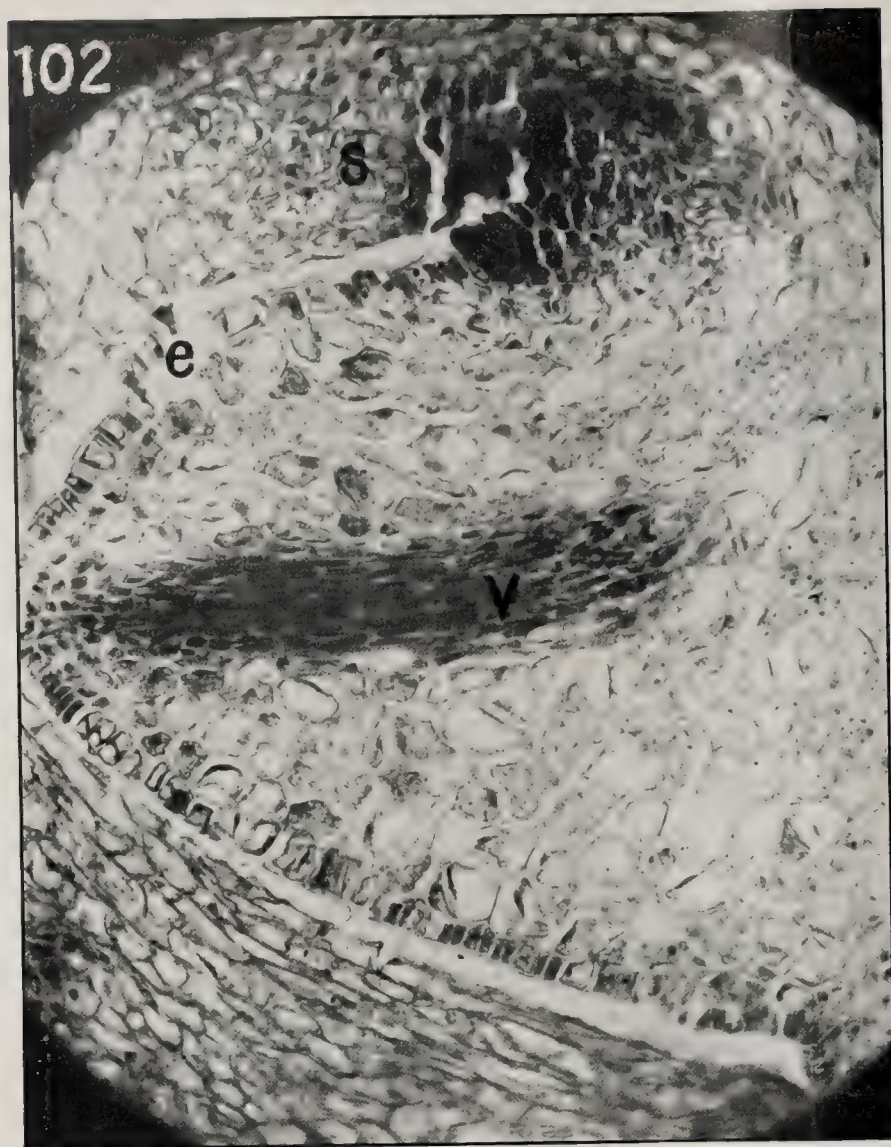


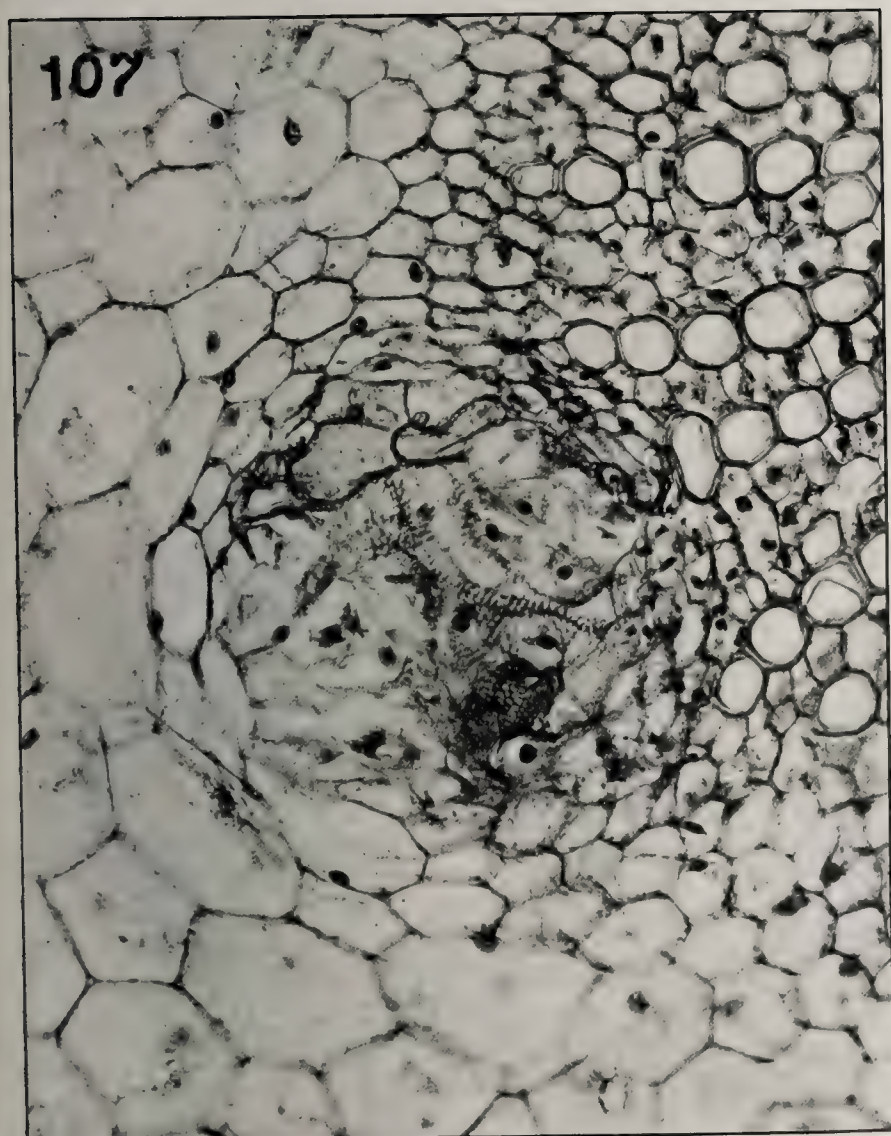












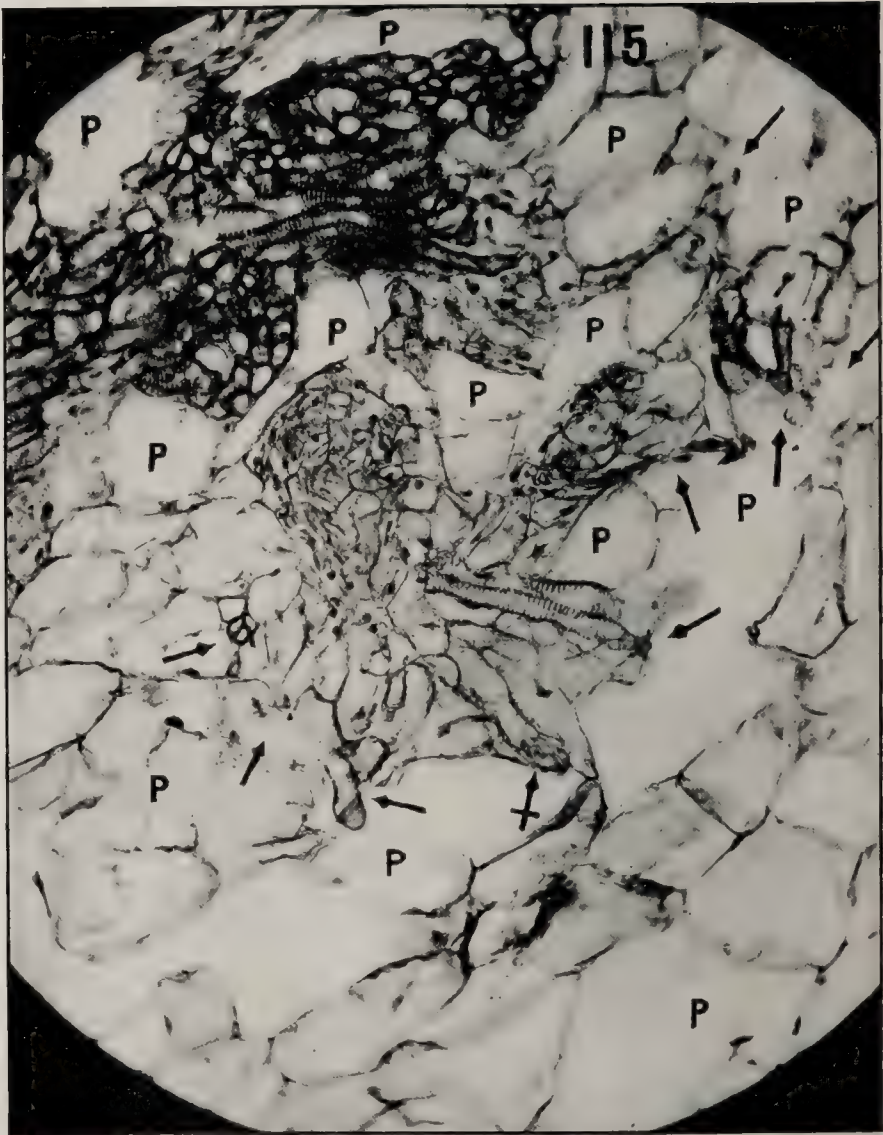
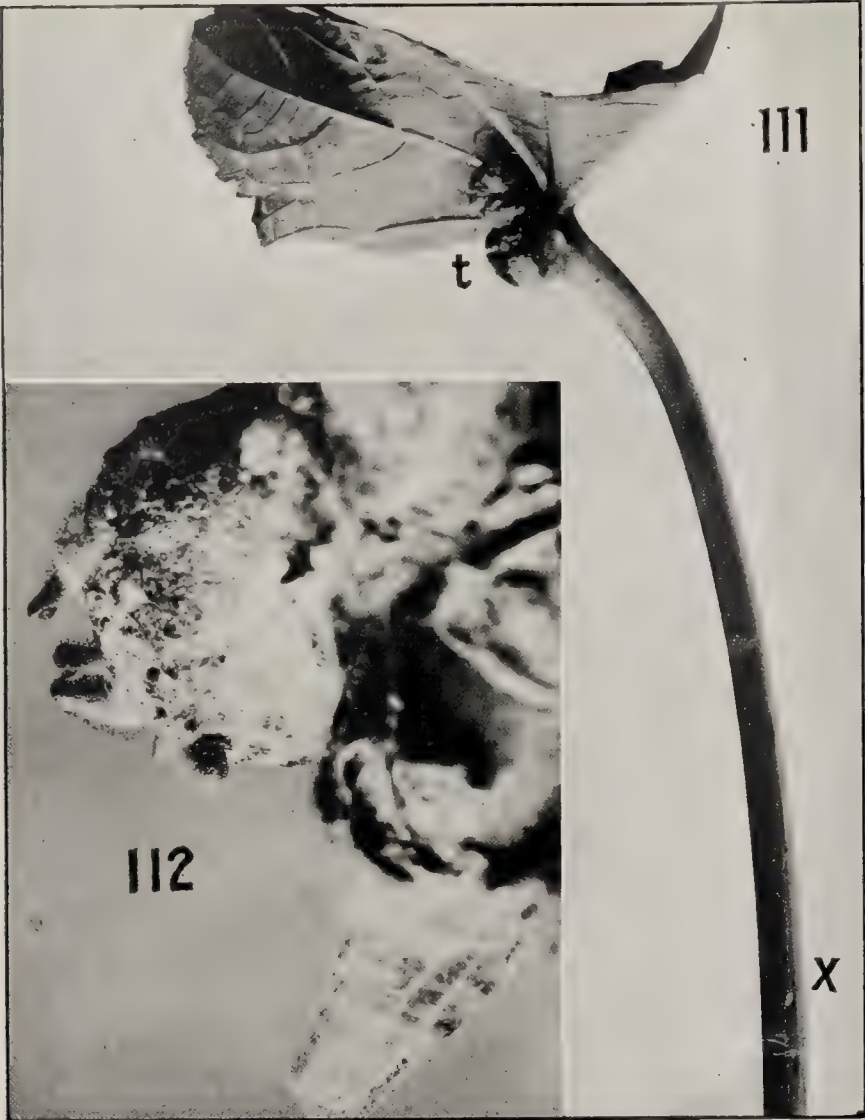


FIG. 78.—Leaf-axil crown-gall teratoids on cauliflower. Inoculated by needle-pricks, September 29, 1916, with the hop strain of *Bact. tumefaciens* (Colony 1 from sunflower inoculation of 1915). Front view. Left tumor commencing to decay. The tumors bear both roots and leafy shoots, the middle shoots being knobby (internally sarcomatous) while the upper shoot on the left-hand tumor is wholly sarcomatous. Photo. January 2, 1917. ($\times 2$ circa.)

FIG. 79.—Back of Fig. 78. Time 95 days. The shoots at the left which looked normal in Fig. 78 are here seen to be tumefied at their base, and the lower one also in its middle part. ($\times 2$ circa.)

FIG. 80.—Pelargonium internodal crown-gall teratoid. Planar enlargement of a section through II of Fig. 60, in the part containing both diminutive leafy shoots and red (floral) pigment. Stem inoculated August 1, 1916, cut and fixed September 6. Slide 1282-19. Cortex and cambium both involved, wood much thickened. The arrows indicate approximately the surface of the cut stem. Cortex on left side, pith on right. Bulk of the tumor sarcomatous. Twisted (somewhat torn) teratoid elements at the top. For details consult Figs. 81 to 87. Figure 86 is from the white area in the center ($\frac{3}{4}$ inch from the top of the plate) and the large grayish, fine-celled mass below it is sarcoma.

FIG. 81.—Pelargonium crown-gall teratoid. Thickened and distorted (criss-crossed) cambium from base of the tumor shown in Fig. 80. Tracheæ on right, sieve tubes on left. Slide 1282-6. ($\times 160$.)

FIG. 82.—Woody whorl in Pelargonium tumor. Tracheæ numerous; sieve tubes on periphery. Slide 1282-6. ($\times 160$.)

FIG. 83.—Two smaller whorls in cortex of same tumor as in Fig. 82, and one field of the microscope above the latter. The left one is quite immature. Slide 1282-6. ($\times 160$.)

FIG. 84.—Mass of deep-staining, sarcomatous tissue lying in modified cortex and connected with the main mass by a pedicle of coarser cells. Slide 1282-10. ($\times 150$ circa.)

FIG. 85.—Central degeneration in Pelargonium teratoid tumor. The white tissue was dead and shriveled in its center when it was fixed. Stained with methyl green and acid fuchsin. Slide 1282-6. ($\times 150$ circa.) Dead tissues do not take the fuchsin stain.

FIG. 86.—Coarse-celled, large-nucleated living tissue (cortex?) near surface of Pelargonium tumor shown in Fig. 80, surrounded by the rapidly proliferating small cells of the sarcoma. Slide 1282-18. ($\times 150$ circa.)

FIG. 87.—Middle of tumor in Fig. 80 showing rapidly proliferating small-celled, sarcomatous tissue which contains a few distorted vessels (tracheæ). Slide 1282-24. ($\times 150$ circa.)

FIG. 88.—Planar enlargement of vertical section of axillary Pelargonium teratoid inoculated October 25, 1915, and fixed February 28, 1916. Block 1187 (second piece), slide 12. The photograph is variously lettered to indicate approximately the location of the following photographs showing teratoid fragments growing from the surface of the tumor (W) and buried in its thickened cortex, which extends as far inward as the middle curved line of xylem (xy), beyond which is modified pith (m) containing many distorted tracheæ (wood vessels).

FIG. 89.—Detail from Fig. 88 at W showing an abortive surface organ. The tumor is naked, sarcomatous and disintegrating at X. At the right are normally oriented cortex cells. Slide 1187-12. ($\times 160$.) The dark part under the sprout is embryonic tissue.

FIG. 90.—Buried embryonic tissue covered by a membrane and lying upside down unconformably on other tissues. The arrow points toward the surface; sarcoma cells at S. Lining membrane at e. In the upper (dark) part, which represents embryonic tissue, epidermis faces epidermis. From Fig. 88 at A. ($\times 150$ circa.)

FIG. 91.—Small fragment of embryonic tissue showing its membrane (epidermis) at e lying unconformably on another tissue. The arrow points toward the surface of the tumor. Block 1187. From Fig. 88 at B. ($\times 200$ circa.)

FIG. 92.—Another small fragment of embryonic tissue, capped by a trichome, and buried unconformably in a second mass of younger embryonic tissue. The surface lies in the direction of the arrow. The best developed part is covered by a membrane; the deep-staining younger part is not covered. The sarcomatous tissue is at s, s. From Fig. 88 at V but from slide 1187-19. ($\times 175$ circa.)

FIG. 93.—Extreme upper left part of Fig. 92 for the sarcomatous portion, and also half a field nearer the surface to show another finger-like portion of the sarcoma lying in the cortex. Slide 1187-19. ($\times 200$.) For orientation in connection with Fig. 92. The finger-like central mass of disorderly cells ends abruptly (like the upper mass) in a coarse-celled cortex $\frac{1}{2}$ inch beyond the right margin of the picture. See upper S of Fig. 92.

FIG. 94.—From Fig. 88 at Z. Lobes of embryonic tissue in cortex. These point toward the surface (s). Their top is covered by a membrane and one of them bears a glandular hair. Slide 1187-12. ($\times 160$.) The dark color is due to the deep red (fuchsin) stain.

FIG. 95.—From Fig. 88 at Y, showing membrane-bearing embryonic fragments lying in cortex; the dark parts are embryonic tissue; x, sarcoma; c, c, cortex. Surface lies in direction of arrow. Slide 1187-12. ($\times 160$.)

FIG. 96.—From Fig. 88 at R, which is two fields of the microscope deeper in the tumor than Fig. 92. It shows small fragments of embryonic tissue (tooth-shaped pieces) bounded by a membrane pointing away from the surface, lying unconformably on other embryonic cells and surrounded by coarse-celled cortex. In the upper dark part at the extreme left vessels are visible. This part ends abruptly in a coarse-celled cortex just beyond the part here shown. Slide 1187-19. ($\times 200$.)

FIG. 97.—From Fig. 88 at S, but on slide 1187-14. Three small tooth-shaped pieces of embryonic tissue covered by epidermis and lying unconformably in cortex. Tissue sarcomatous at S. The surface lies in the direction of the arrow. ($\times 200$.)

FIG. 98.—Embryo fragments in cortex near surface of tumor. Sarcoma at S but mostly out of focus. Block 1187. Slide misplaced, probably near No. 14 or No. 15. Possibly 17. ($\times 160$.)

FIG. 99.—From Fig. 88 at T. Slide 1187-12. Deep-staining embryo fragments lying unconformably in cortex. ($\times 150$ circa.)

FIG. 100.—Longitudinal radial section through outer normal part of a Pelargonium stem (below a tumor) for comparison with Figs. 82, 84, 86, and enlarged (tumefied) cortex shown in Fig. 101. This shows surface (cork layer) at the left and then the ordinary cortex cells of the young stem. Trichome at T. Slide 1282-24. ($\times 150$ circa.)

FIG. 101.—Outer part of overgrown cortex of a Pelargonium teratoid tumor. Plant inoculated October 19, 1915, and material fixed January 11, 1916. Surface of tumor at right covered by an irregular epidermis bearing hairs. The cells are smaller than normal cortex cells (Fig. 100) and many are filled with starch, but are normally oriented or nearly so. The excess of starch means that more sugar passed into the tumor than could be used for growth, the surplus in such cases being converted into starch and stored as a harmless product. Sarcomatous elements occur at S, S. Slide 1166-15. ($\times 150$ circa.)

FIG. 102.—Slide 1166-15 immediately under (at left of) Fig. 101. It shows a small tooth-shaped piece of tissue (a bud) pointing exactly away from the surface of the tumor. This has a well developed epidermis (e) and incipient vessels (V). Sarcoma cells occur at S. The tissues above and below this bud are shown in Figs. 103 and 104.

FIG. 103.—Photomicrograph from slide 1166-15 immediately above Fig. 102, showing disorderly (sarcomatous) arrangement of the cells. At the top on the right are cortex cells (C). The dark cells in the extreme lower part (e) are deep-staining normally oriented embryonic cells, i. e., the same as those shown in the upper part of Fig. 102. The rest of the tissue is sarcomatous. ($\times 180$ circa.)

FIG. 104.—Slide 1166-15 immediately below Fig. 102, a small portion of which is included at the top. This field also is largely sarcomatous. ($\times 160$.)

FIG. 105.—Same tumor as in Fig. 104, but from another part nearer the surface. The section shows on the left the deep-staining, imperfectly vascularized, disorderly cells of the sarcoma, and on the right the non-sarcomatous but overgrown cortex. Slide 1166-22. ($\times 180$ circa.)

FIG. 106.—One lobe (enlarged) of that part of the nasturtium tumor shown at Z in Fig. 76. Numerous roots can be seen pushing out of the otherwise naked body of the tumor. A little of the stem is visible at the extreme left. Inoculated August 5, 1916. Photo. November 13, 1916. ($\times 6$.)

FIG. 107.—Paris daisy stem between tumors, in cross-section, showing outer part of pith (at left) and inner edge of vascular bundle. In the center of the figure is a tumor strand here consisting mostly of disoriented pitted vessels (tracheæ) to the right of which are the normal spiral vessels and medullary rays of the inner face of the bundle. There are normally no tracheæ in this part of the bundle. The black dots are nuclei. Slide 639-A-19. ($\times 210$.)

FIG. 108.—Inoculated crown gall on rose. Not a teratoid. The organism used was isolated from tumor on a hot-house rose received from Massachusetts. Inoculated June 2, 1916. Photo. September 21, 1916. (Natural size.)

FIG. 109.—Massachusetts gall on rose. The primary tumor, XX, was produced by a bacterial inoculation made June 16, 1916. This tumor was treated January 10, 1917, with a caustic oil and destroyed, but new tumors have arisen from its base. Photo. May 16, 1917. (Natural size.)

FIG. 110.—Paris daisy stem killed by crown gall. It was inoculated April 7, 1911, at X, X, from a colony plated from a secondary gall. Tumors developed at the sites of inoculation and later sloughed off. Subsequently a new tumor appeared at Y. This tumor, together with the whole stem, was dead when the photograph was made, January 23, 1912. Time 10 mos., nearly.

FIG. 111.—Ricinus leaf inoculated on the blade with the hop strain of the crown-gall organism. Tumors at t on both upper and under surface of the blade. X is the level of the cross-section shown in Figs. 68, 69. (Natural size.)

FIG. 112.—Pelargonium stem teratoid showing glandular, hairy, abortive red outgrowths (floral anomalies) protruding from the surface of the tumor. This is a side view of Plate XV, Fig. 57, in *The Journal of Cancer Research*, April, 1916.

FIGS. 113, 114.—Figures showing imperfect development of one side of a secondary tumor in the petiole of an inoculated Paris daisy. The larger cells are the normal cells of the cortical parenchyma of the leaf stalk. Surface of petiole at right in 113 and at left in 114. Slide 590-B-13. ($\times 160$.)

FIG. 115.—Margin of crown-gall tumor from inoculated disk of the sunflower. The tumor is an extremely vascular growth developed from the torus (thin vascular layer which bears the seeds), but lying in the pith. The whole is an invasion. P, P, designate pith cells and the arrows the marginal advancing portions of the tumor stroma and tumor cells. Some of the vessels are so young as still to lack woody deposits and still to contain nuclei, as the one designated by the crossed arrow. Slide 1147-C-6. Stained with acid fuchsin and methyl green—sarcoma cells red, vessels blue, pith cells white. ($\times 160$.) May be compared with Figs. 6 and 52 of my paper in *The Journal of Cancer Research* (April, 1916), which were made from the same series of sections.

THE CARREL TREATMENT OF WOUNDS APPLIED TO CIVIL PRACTICE.

By JOS. S. LAWRENCE, A. M., M. D.,

With the American Ambulance, Neuilly, France, Summer, 1916.

The Carrel-Dakin method of treating infected wounds depends for its success so largely upon the technique with which it is applied, that it seemed advisable to write out carefully the various steps, paying particular attention to the bacteriological phase. The surgical phase has been treated exhaustively in a number of recent articles, but the bacteriological part has usually been stated very briefly. It is very necessary that careful attention be given to the bacterial content, which should be regularly ascertained, as a guide for the surgeon. Secondary infection may readily occur after the wound has been under treatment even in the hands of the most skillful attendants, and for its detection the bacteriological charts are found more serviceable than the temperature records. The method here described is simplified so that it may be used for the treatment of one case or of many cases, for its employment in hospitals or for use in the dispensary or office on ambulant patients. It is the technique which is employed in The Johns Hopkins Hospital.

In order to secure satisfactory results from the employment of the Carrel method, it is absolutely necessary that the following points be given the strictest attention. First, Dakin's solution, the fluid used for irrigation, must be very carefully

prepared according to the formula described by Daufresne.¹ It breaks down readily when exposed to the light or air and hence should be kept well corked in colored glass bottles, never in metal containers. A preparation more than a week old should not be used. This solution is not a powerful disinfectant but a mild antiseptic. Second, this is not a system of drainage, but of irrigation or laking. Third, a knowledge of the efficiency of the treatment can be obtained only by systematic, accurate and careful bacteriological observations.

The method can be employed with success in the treatment of most flesh wounds, abscesses, compound fractures or chronic osteomyelitis. We feel strongly that it can be used and is indicated in most cases where at the present time drainage is instituted. It may be considered prophylactic or therapeutic according to the nature of the case. If the wound has been freshly made in sound tissue, the object will be to prevent the development of infection; but if the case is one of chronic abscess or osteomyelitis, the aim is to eradicate the infection. The steps in the method are about as follows: If the wound is the result of an accident and is filled with dirt,

¹ J. A. M. A., 1916, Dec. 9, LXVII, 1777.

shreds of clothing and other foreign bodies, all of the débris should be removed with forceps and by scrubbing with green soap and sterile water. A brush can be used for this purpose if necessary, and shreds of tissue that are without a blood supply should be excised. If we have a puncture or penetrating wound that is more extensive beneath the skin than on the surface, it should be opened so that thorough irrigation may be established. The object here is to prevent the multiplication of any bacteria in any part of the wound among the many that were carried in by the accident. In the presence of Dakin's solution, when properly made, no bacteria can flourish, their development is inhibited, while the body tissues are not hindered in their repair work. Phagocytosis, as a rule, is observed to take charge of the introduced organisms. Healing of the wound by first intention can be expected in many cases. If, however, the wound is more than six hours old, or we have a chronic sinus discharging pus, the problem is a little more difficult. The wound should be thoroughly cleansed, foreign bodies removed, necrotic tissue cut away and the surface opening increased, if necessary, in order to secure the best results from the irrigation. A counter opening should be avoided when possible in deep wounds, and in penetrating wounds the perforation farther from the main injury should be encouraged to close early. The object is always to secure thorough flooding of the injured tissues at each irrigation. To help to insure this, a certain type of rubber tubing, with a caliber of about 4 mm., is used for insertion. It is tied off at one end and perforated at this end with from eight to twelve holes made with a No. 4 leather punch, the first hole being placed as near to the tie as possible and the others arranged spirally and about half an inch apart. Such a tube insures a better spreading of the irrigating solution in a large wound or over a surface wound. If it is a narrow sinus that is to be irrigated, a plain tube open at the distal end and not perforated may be employed. All tubes must be free to move around and must under no condition be packed in with gauze, nor should the surface of the wound be closed in over them. If they are fixed in one position for more than 24 hours the bacteria will multiply rapidly in their bed beyond the irrigating holes. If they are packed in between pads of gauze the bacteria will flourish beneath the gauze, inasmuch as the mechanical effect of the irrigating solution is lost to those parts. The surface must not be closed, for then the free discharge of the surplus fluid and its burden of pus and bacteria will be prevented and any pressure on wounded tissue may produce necrosis, thereby increasing the opportunity for bacterial development. The irrigation should be of sufficient amount to flood the entire wound and a little more, so that the wound may be washed at each irrigation, but care should be taken not to use so much that the outer dressings or the bed are wetted. The irrigations must be made every two hours. A longer interval will permit the dressing to dry in some instances, thus giving an opportunity for bacterial development, whereas a shorter interval will permit too great a flooding of the wound and an irritation of the skin from wet dressings in some patients. The continuous drip was found to be undesirable. Under no condi-

tions should the dressings be removed by any but the attending surgeon, and then only under the strictest antiseptic conditions; usually one dressing a day is sufficient and, when the wound is almost healed, the dressing may be done at two-day intervals if the surgeon is pressed for time. From the beginning of the treatment the wound should be treated as a sterile wound. Only the most accurate aseptic technique will succeed. *Reinfection is always possible either with the same or with different organisms.* This point cannot be emphasized too forcibly, for while the reinfection may not be accompanied with clinical symptoms, yet the implantation of new organisms reproduces the complex conditions of combined infections and

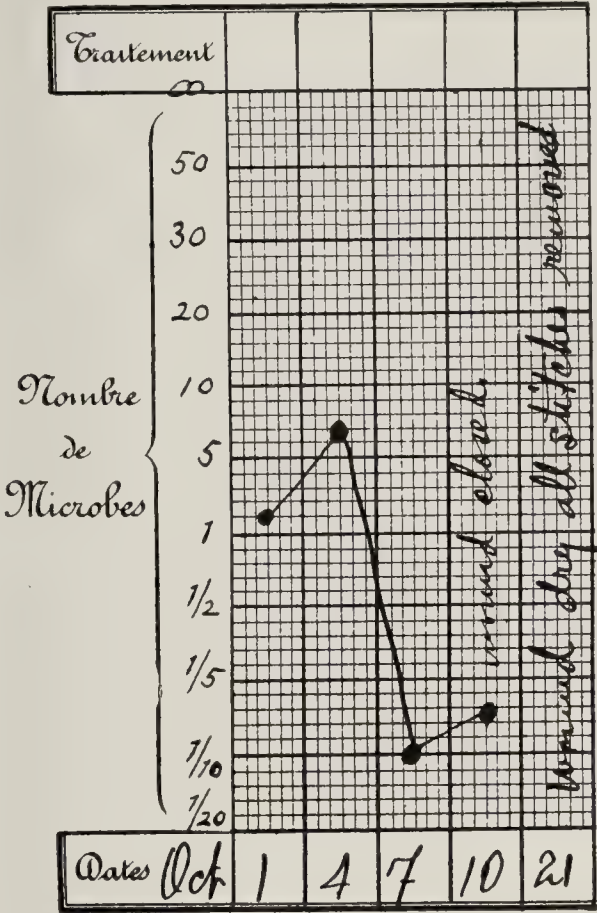


CHART I.
COMPOUND FRACTURE OF THE RIGHT RADIUS.

The wound was cleaned in thirteen days. For at least four of these days the bacterial count was less than one organism in five fields. On October 10, the edges of the wound were freshened and stitched tight. On October 21, the stitches were removed and the patient discharged to a convalescent hospital with only a simple fracture.

postpones the day of recovery. The more nearly every wound is treated as though exposed to infection, just as the wound made by the surgeon in operating is exposed to infection, the more satisfactory will the results be. The irrigation can be done by a nurse without disturbing the patient, even while the patient sleeps at night, and this two-hourly interval must be observed throughout the 24 hours. Partly to protect the wound from infection by organisms on the skin and partly to protect the skin from irritation by the Dakin's solution, strips of gauze about four inches wide, previously steeped in sterile vaseline and picric acid, are spread over the skin about the wound, covering every part of the skin but not any of the

wound or granulating surface. The hair in the neighborhood of the wound is kept shaved close to the skin.

The fact that we are aiming to irrigate and not to drain must be kept in mind when we are placing the tubes; they should be placed so as to take full advantage of gravity when irrigating. If they are pushed up into the wound with the outer end extending down, it will be much more difficult to get fluid through to the wound and as much of the fluid as fills the tube will never reach the wound but drain immediately after the pressure is removed. Dakin's solution to retain its efficiency must be protected from light and air, and under no condition should it be warmed. If the free chlorine contained

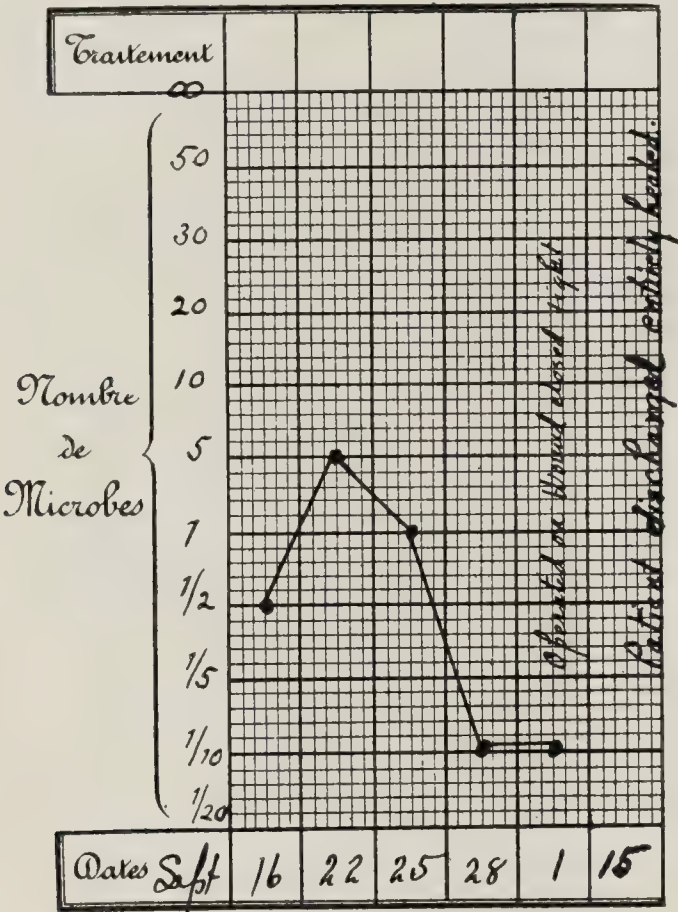


CHART II.

COMPOUND FRACTURE OF THE MIDDLE OF THE LEFT HUMERUS.

In twelve days the bacterial count was brought to one organism in ten fields. After four days the edges of the wound were freshened and stitched. On October 15, the patient was discharged with only a simple fracture.

is the active principle of the solution, exposure to air or light or heating the solution will liberate this and therefore impair the efficiency of the treatment.

At the time of the dressing, a thorough irrigation of the wound is advisable both to determine that the tubes are open and working properly and to remove any debris that may have collected. If the surface of the wound is not clean, it should be cleaned with a dry sponge. To keep the tubes from slipping out of the wound they are fastened to the skin with adhesive tape, and sponges wet with the solution are placed loosely over them on the surface of the wound. Dakin's solution dissolves fibrin very readily, thus clearing away and carrying off the fibrin in the pus that might otherwise be deposited. But it

also dissolves the fibrin of a blood clot and thus, if a large vessel is ruptured in the wound, treatment with Dakin's solution may be the cause of a secondary hemorrhage.

On every other day an inspection is made of the bacterial content both as to number and variety. No irrigation is permitted for at least two hours preceding this dressing. With a sterile platinum spatula a bit of material is taken from the most vicious part of the wound or, if the wound looks uniformly good, specimens are taken from several points. The spatula must be sterilized each time just before it is applied to the wound. The material is spread in a thin film over a glass slide and allowed to dry. The film should not be too thick,

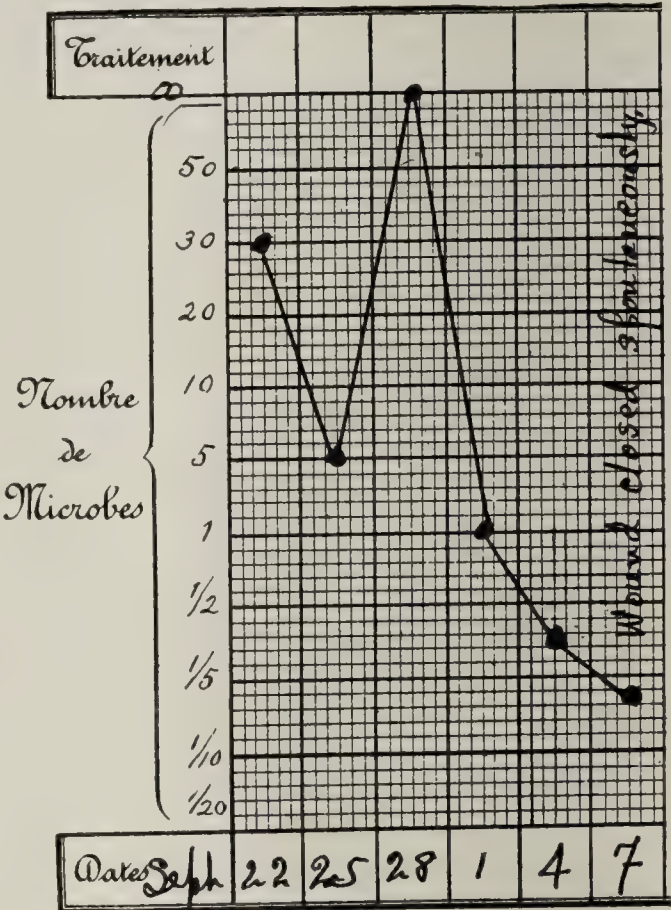


CHART III.

COMPOUND FRACTURE OF THE LEFT SUPERIOR MAXILLARY BONE.

This wound, after it had been cleaned, closed spontaneously and healed without stitching.

otherwise it may be too dense for examination. In the laboratory this film is stained with methylene blue and examined with an oil-immersion lens. A certain amount of experience will accustom the examiner to choose fields of a certain density as standard. These fields should have the pus cells arranged in a single layer and uniformly covering the whole field. The number and variety of organisms are noted. The noting of large and small bacilli, staphylococci and streptococci, is a sufficient distinction as to variety. In counting, no attention is paid to variety but the organisms are counted as a whole. If there are a hundred or more germs in the field, a second and third field are examined; and, if these, too, show great numbers, the count is said to be "infinity," and no further examination is necessary. If, however, there are only five or

ten organisms in the first field, then five other fields in different parts of the slide are examined, the total count of all the fields is averaged and this average taken as the count. If the bacterial content is still poorer, perhaps only one or two to a field, at least 10 fields are examined, and when the count is lower than this, 20 or more fields are searched. It often occurs in this latter phase that 10 or 15 fields may be examined without a single organism being noted, and then in the next field a phagocyte will be found which has engorged a score or more of organisms. These phagocytized bacteria are counted or estimated and averaged in the same manner as though the organisms had been scattered extracellularly. The results of these examinations are charted on sheets similar to temperature charts and always kept at hand for the surgeon's inspection. These observations are the index to much valuable information. First, they tell the nature and extent of the infection and whether it is spreading or receding. Later, as parts of the wound clear up, the counts tell which part is not receiving its regular irrigation. If a corner of the wound is blocked off by a gauze packing, the bacterial content of this part will be much higher than that of other parts receiving their regular irrigation. In general, it has been observed that the count drops from infinity to 10 or 20 per field within the first 24 or 48 hours if the irrigation is satisfactory; but if this drop is not observed, a thorough inspection of the technique should be made at once. If this shows no fault, then the wound should be examined for

an unexplored and unirrigated pocket. Second, this observation enables one to discover a reinfection before it has become extensive. A sudden rise of the count or the discovery of new organisms indicates a reinfection either from the evacuation of a pocket of pus or from an outside source. Immediate re-establishment of the full irrigation may control this inoculation in a few hours. When the count averages one organism or less to five oil-immersion fields for a continuous space of six days, the wound is considered bacteriologically clean. A certain percentage of such wounds have shown themselves to be absolutely sterile on culture. When surgical repair work is indicated, it can be done at this time as safely and with as much ease and security as though the wound were fresh. The previous infection can be completely ignored.

The great advantages of the Carrel method of treating infected wounds may be summed up as follows: It successfully checks the extension of the infection, causes an almost immediate drop of temperature and brings comfort to the patient. Pus is eliminated and dressing simplified. An early opportunity is given for surgical repair work. The production of cicatricial tissue is minimized and the interference with function of the part is less after the recovery of the patient. Finally, it is a scientific and intelligent method of observing the process of healing in wounds and determining the efficacy of treatment.

PLACENTAL TRANSMISSION: TOTAL CREATININE IN PLASMA, WHOLE BLOOD AND CORPUSCLES OF MOTHER AND FETUS. (ADDITIONAL ANALYSES BY A NEW METHOD.)

By E. D. PLASS.

(From the Department of Obstetrics, Johns Hopkins University and Hospital.)

In a recent study of the placental transmission of creatinine and creatine, it was found that the maternal and fetal plasmas or sera have the same concentrations of these two substances, but that the whole bloods show the same definite relationship only in the preformed creatinine, whereas the total creatinine and subtracted creatine values are higher in the fetal bloods.¹ It was suggested that the values obtained for total creatinine in whole blood by Folin's method were probably too high. Subsequent observations have indicated that this criticism is valid and by the use of the acetic acid precipitation method, lately suggested, consistently lower results were obtained.² The higher values found when the Folin procedure is employed are probably explained by the presence in the blood of some substance, not creatine, which when heated with picric acid, produces a compound which gives a color development on alkalization similar to that produced by creatinine.

In continuing the previous work, a number of determinations of total creatinine were made on plasmas and whole bloods by means of the new procedure. The preformed creatinine was not determined because the previous analyses had indicated that if the blood is unhemolysed the two samples

give approximately the same results. In view of the reported lower creatine content of fetal tissues^{3, 4, 5} it seemed probable that the blood cells would show a comparable difference, but such was not the case.

The specimens were collected as in the previous experiments. The hematocrit values were determined by direct centrifugalization of the undiluted whole blood. A known quantity of whole blood or plasma was precipitated by heat and .01 N acetic acid and the filtrate cleared with a suspension of aluminium hydroxide. The second filtrate was evaporated to 5 c. c. on a water-bath and taken up with hot water, the total volume being kept at approximately 10 c. c. One cubic centimeter of 5N HCl was added and the solution heated on a water-bath for from 3 to 4 hours, after which it was neutralized with 20 per cent NaOH and 20 c. c. of 1.2 per cent picric acid were added. Next there were introduced 1.5 c. c. of 10 per cent NaOH to develop the color, and after 10 minutes the solution was diluted to 50 or 100 c. c. and the color compared with that produced by a known amount of creatinine treated similarly.

The results in a series of 12 sets of plasmas or sera are essentially the same as those previously obtained by the use of

Folin's method, and the agreement between the maternal and fetal samples confirms the view that the placental transmission of the creatinine bodies is by simple diffusion. The actual findings are recorded in Table I; a statement as to the presence or absence of hemolysis is included to emphasize the fact that the presence of hemoglobin does not materially affect the results obtained by the use of this method.

TABLE NO. I.
TOTAL CREATININE IN MATERNAL AND FETAL PLASMAS.
(Mg. creatinine in 100 c. c.)

Source.	Maternal.		Fetal.	
	Hemoglobin.	Total Creatinine.	Hemoglobin.	Total Creatinine.
Case No.				
26	0	1.74	0	2.04
29	0	1.65	+	1.85
30	0	2.02	++	2.31
31	0	1.69	+	1.72
32	+	1.90	++	1.90
33	0	1.80	+	1.79
34	+++	2.06	++	1.75
35	+++	1.62	++	1.63
36	++	1.39	++	1.27
40	+++	1.16	+++	1.15
41	0	1.19	+	1.40
43	+++	2.12	+++	2.00
Average		1.70		1.73

Ten sets of maternal and fetal whole bloods were analyzed, and in seven the plasmas were also available. The results are tabulated in Table II, as are also the calculated total creatinine contents of the corpuscles expressed in milligrams per 100 c. c. Here, again, we find the same concentration in the plasmas of both mother and child.

The amounts of total creatinine in the whole blood and corpuscles, however, do not show any such parallelisms. The quantities in the maternal whole blood are higher in three instances, in the fetal in six, and in one (No. 36) there is no difference; the average contents are quite comparable. The calculated corpuscular content is higher in the maternal sample in five cases, in the fetal in three, and in two only a slight difference is noted. The age, color and parity of the mothers, the sex and weight of the children, the duration of labor and various clinical details were tabulated, but gave no suggestion regarding the reason for the observed variations. Until some explanation for these differences of storage in the blood cells is proposed, no attempt can be made to correlate the findings here recorded.

As the preformed creatinine seems to be present in small and rather uniform quantities in both plasma and corpuscles, the relatively large amounts of total creatinine are apparently due to a storage of creatine. Many of the tissues of the body contain creatine, but very little creatinine, and it is not surprising that the blood cells can store small quantities of the former substance. In the non-pregnant state this storage is apparently smaller (6.2-6.5 mg. per 100 c. c.) than during pregnancy, whereas in the male a single determination showed a still lower concentration (4.9 mg. per 100 c. c.). In the tabulated series in only one instance (Case No. 41) is there no

evidence of a considerably increased storage; whereas the average figures are nearly double the normal. There are no available figures bearing upon the relative concentration of

TABLE NO. II.
TOTAL CREATININE IN WHOLE BLOOD, PLASMA AND CORPUSCLES.
(Mg. creatinine in 100 c. c.)

Source.	Maternal.				Fetal.			
	Hemato-crit.	Whole Blood.	Plasma.	Corpuscles.	Hemato-crit.	Whole Blood.	Plasma.	Corpuscles.
Case No.								
34	31	6.16	2.96	15.29	34	5.03	1.75	11.38
35	37	4.76	1.62	10.11	52	5.40	1.63	8.88
36	32	5.33	1.39	13.69	44	5.37	1.27	10.59
37	31	4.44	1.70*	10.55	30	5.67	1.70*	14.93
38	28	5.41	1.70*	14.96	29	5.67	1.70*	11.14
39	34*	4.91	1.70*	11.15	40*	4.47	1.70*	8.63
40	33	3.40	1.16	7.94	42	4.42	1.15	8.93
41	39	3.06	1.19	5.99	44	3.56	1.40	6.32
43	37	5.55	2.12	11.38	42	6.25	2.00	12.12
44	39	3.65	1.35	7.26	43	5.92	1.35†	11.98

* Actual determinations not made—average values taken.
† Not determined—maternal value used.

creatine in the muscle and other tissues in the non-pregnant state and during gestation, so it cannot be said whether this phenomenon of creatine storage is general or affects only the blood cells.

SUMMARY AND CONCLUSIONS.

Previous work on the total creatinine content of maternal and fetal plasma and whole blood was repeated, a different analytical procedure being employed. No definite relationship has been shown to exist between the maternal and fetal whole bloods in a given case, but the plasma values in both series of experiments agree closely, indicating a direct diffusion of the creatinine bodies through the placenta.

In the parturient woman and in the new-born child there is usually an increased ability of the red blood cells to store creatine. In spite of the reported lower creatine content of fetal tissues, the maternal corpuscles do not always show a higher creatine content than the fetal cells.

BIBLIOGRAPHY.

1. Plass, E. D.: Placental transmission: creatinine and creatine in the whole blood and plasma of mother and fetus. *Bull. Johns Hopkins Hosp.*, 1917, XXVIII, 137.
2. Wilson, D. W., and Plass, E. D.: Creatine and creatinine in whole blood and plasma. *J. Biol. Chem.*, 1917, XXIX, 413.
3. Mellanby, E.: Creatin and creatinin. *J. of Physiol.*, 1907-8, XXXVI, 447.
4. Mendel, L. B., and Leavenworth, C. S.: Chemical studies on growth. Notes on the composition of embryonic muscular and nervous tissues. *Amer. J. of Physiol.*, 1908, XXI, 99.
5. Rose, W. C.: Excretion of creatine in infancy and childhood. *J. Biol. Chem.*, 1911-12, X, 265.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

It is issued monthly. Volume I begins with January, 1917. The subscription price is \$3.00 per year. (Foreign postage, 50 cents.) Price of cloth-bound volumes, \$3.50 each.
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Orders should be addressed to THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

NOTES ON NEW BOOKS.

Hand-Book of Venesection. By WALTON F. DUTTON, M. D. Cloth, \$2.50. (Philadelphia: F. A. Davis & Co., 1916.)

This small volume, of about two hundred pages, is an attempt to present to the profession an epitome of the indications for venesection, with a broad discussion of the physiological effects that may be obtained in each instance.

The first forty pages are devoted to a fascinating history of Bloodletting, taken from a paper by Fielding H. Garrison, read before the Medical History Club of Washington, D. C.; on December 30, 1911.

The remainder of the book consists of a category of diseases which may be treated by venesection or which have been so treated in the past. The discussion of the physiology of disease is largely good, though one is struck by the undue emphasis placed by the author upon vasomotor disturbances of the cerebral circulation. Such disturbances, the author claims, are the cause of epilepsy which should be treated by venesection. A chapter is devoted to hypertonia vasorum cerebri, which seems to be an entirely hypothetical condition, but which is, nevertheless, to be treated by venesection.

The author advocates, with good physiological reasoning, the use of venesection under certain circumstances in aneurism, emphysema, angina pectoris, cerebral hemorrhage, asphyxia, arteriosclerosis, pneumonia, eclampsia, gout with uremia, pulmonary edema and congestion, uremia and various cardiac conditions. He places proper emphasis upon dilatation of the right heart, cyanosis, and venous engorgement as being of primary importance for the indication of venesection.

The book is, however, that of an enthusiast, and one is startled by the list of conditions which are to be treated, under some circumstances, by venesection—rheumatism, syphilis, obesity, migraine, hypertonia vasorum cerebri, typhoid fever, epilepsy, psychopathic states, hypertension, etc.

The technique of venesection and of transfusion as described by the author belongs to the surgical procedures in vogue a few years ago, and no description is given of the new and much more readily applicable methods of venesection and transfusion through needles.

The book is interesting but somewhat optimistic as to therapeutics by venesection. J. T. K., JR.

The American Year-Book of Anesthesia and Analgesia. Edited by F. H. McMECHAN, A. M., M. D. Cloth, \$4.00. (New York: Surgery Publishing Co., 1915.)

The American Year-Book of Anesthesia and Analgesia is made up of a collection of articles by prominent authorities on this subject. The table of contents shows an impressive list of contributors from all over the States and from England as well, with papers covering the subject from all aspects, from the deeply scientific to the extremely practical. It will prove of great interest to anesthetists rather than of actual value to the student who is giving his first anesthetic. The papers are slightly contradictory on some points which goes to show that there is much about the subject that has yet to be brought down to indisputable fact. It is interesting to find one of the articles by a lay woman whose point of view coincides with that of most patients and should be respected and born in mind constantly. Those who read this year-book will anticipate with eagerness next year's volume.

Diseases of the Nose and Throat. By ALGERNON COOLIDGE, A. B., M. D. Cloth, \$1.50. (Philadelphia: W. B. Saunders Co., 1915.)

This little book fills its purpose admirably. As stated in the preface, it purports to be only a manual and does not attempt any complete discussion of the subject.

The words are well chosen, the sentences are short and concise. The subject matter is, on the whole, quite accurate, though certain phases do not receive the importance they deserve. For instance,

the relation of sinus infection to asthma is not altogether clear. The indications for tonsillectomy are clearly expressed and complete. There is an excellent table treating of the differential diagnosis between syphilis, tuberculosis and malignant neoplasms.

The illustrations are all schematic, but give the student a very good idea of anatomical relations. The author has very wisely omitted all illustrations of instruments and discussions of various methods of operations. This is quite a departure from the ordinary book on this subject and is a great relief. A concise table of contents and index add greatly to the value of the book from the student's point of view.

H. R. S.

Diagnostic Methods: Chemical, Bacteriological and Microscopical. By RALPH W. WEBSTER, M. D. 5th Edition. Cloth, \$4.50. (Philadelphia: P. Blakiston, Son and Co., 1916.)

The fact that this book has gone through five successive editions since 1909 is in itself testimonial enough as to its contents and its value in practical clinical medicine. The author is to be congratulated for the zeal which prompts him to keep abreast with all valuable advances in the line of clinical laboratory methods to such an extent that a new edition can be published in each of four successive years. Despite the curtailment of scientific investigation as one result of the war, a sufficient amount of new material has been brought together in this present volume to give the book 725 pages of text in which can be found practically all acceptable methods for the analysis of the ordinary laboratory specimens. The arrangement of the subject matter is orderly and logical, the descriptions of methods are uniformly clear and singularly free from error. Included in the subject matter are numerous references of value to the original literature. The author is to be congratulated upon his obviously successful effort to keep this book foremost among those dealing with the subject of clinical microscopy.

S. R. M.

The Healthy Girl. By MRS. J. CUNNING, M. B., and A. CAMPBELL, B. A. Cloth, \$1.75. (Oxford University Press, London, 1916.)

Written by authors possessing a good insight and understanding of the growing mind and body, this book is intended for the growing girl and those adults who have her welfare in charge. The greater part of it, however, is better adapted to the adult than to the growing girl herself. A concise, common sense and very practical survey of the anatomy and physiology of the human body in their relation to health and disease is given in a simple and easily understood manner. A number of illustrations help to elucidate the text. The weak points in the book are to be found in the attempts to give medical advice. The common diseases are briefly described and treatment in some cases is suggested: "use mufflers for sore throats, use a hot-water bottle for appendicitis and in general for any illness where a girl complains of severe pain." "Coffee is a laxative." "In scarlet fever swab the throat every few hours with 1-30 carbolic." The necessity of a doctor's advice in all illness is, however, repeatedly emphasized. The personal hygiene of the growing girl is well handled and the question of regulation of exercise, work, bathing, sleep and fresh air is ably discussed with helpful suggestions as to the planning of the daily routine.

M. D. B.

Nervous Asthma. Its Pathology and Treatment. By J. B. BERKHART, M. D. Price, 2 shillings and 6 pence. (Oxford University Press, London, 1916.)

According to the author two distinct types of asthma are usually grouped under the name bronchial, spasmodic or nervous asthma. Both types, he believes, are the consequence of rickets with its resulting crippling of the thorax and arrested lung development. In the one form, which he designates as actual bronchial asthma, the dyspnea arises from transient obstacles in the bronchial tree—obstacles resulting from the "presence of a tenacious pathological product associated with a defect in the power of expectoration."

In the second form, described as true nervous asthma, no real mechanical obstacle to breathing is supposed to exist, but a neuropathic constitution, with its associated hypersensitiveness to all stimuli, is always present. Furthermore, in all these nervous cases there is a history of childhood inflammatory affections of the air passages and the author believes that these organs, therefore, probably afford a stimulus sufficient to stir up the underlying pathological constitution. Many cases, however, he thinks are pure anxiety neuroses. He lays great stress upon the benefit derived in all cases of nervous asthma from the treatment of the underlying neuropathic constitution by means of proper hygiene, change of surroundings and freedom from solicitous friends. His statements are emphasized by frequent recitals of case reports.

The section of the book dealing with the pathology of the condition is the weakest. The author makes dogmatic statements without attempting to give any evidence. His pathological ideas are unusual and are not presented in a manner which would tend to convert others to his way of thinking.

Principles and Practice of Obstetrics. JOSEPH B. DE LEE, M. D.
Second edition. Cloth, \$8.00. (Philadelphia: W. B. Saunders Co., 1915.)

Dr. De Lee's book is enjoying a well deserved popularity and it has undoubtedly proven itself to be a valuable practical work on the subject of obstetrics.

At times the author perhaps shows a tendency to be rather too dogmatic, as, for example, in his discussion of the life history of the corpus luteum where he hardly gives proper consideration to the more generally accepted view in regard to the origin of the lutein cells.

The chapters devoted to the physiology of labor are particularly good. The various pathological conditions which may arise during the course of pregnancy, labor and the puerperium are discussed

at length, but more particularly from their practical aspects. Although the scientific side has not been neglected, it does not seem that the author has drawn sufficient attention to the numerous unsolved problems existing in scientific obstetrics, which will offer a fruitful field for investigation for a long time to come.

In the section on operative obstetrics, the author describes with great clearness and detail the various steps employed in the operative procedures employed in modern obstetrics.

The book is profusely illustrated with particularly clear and instructive illustrations and diagrams.

In the bibliography, it seems that it would have been an advantage to give with uniformity the titles of the various articles referred to.

Dr. De Lee's book should continue to prove itself to be of great practical assistance to the student and practitioner. K. W.

The Difficulties and Emergencies of Obstetric Practice. COMYNS BERKLEY, M. D., and VICTOR BONNEY, M. D. Second Edition. Cloth, \$7.50. (Philadelphia: P. Blakiston's Son & Co., 1915.)

In the second edition of this work, the authors follow along the lines laid down in the first edition and discuss only the abnormalities encountered in obstetric practice. That there is a distinct field for such a work is proven by the speedy exhaustion of the first edition.

The various obstetrical complications are discussed in much greater detail than is possible in the ordinary text-book on obstetrics.

The section describing the various obstetrical operations is excellent. The book contains numerous illustrations which are unusually clear and instructive, a number of them being entirely new.

The work should continue to prove of value to the student and to the practitioner. K. W.

AN APPEAL TO THE MEDICAL PROFESSION OF THE UNITED STATES.

The Surgeon General's Office has appealed to the medical press of this country for aid in securing the quota of physicians necessary for the care of the great army now in course of organization.

The Medical Departments of the Government are responsible for the examination of the recruits, the hygiene of camps and the care of the sick and wounded. The Surgeons General have not as yet been given full authority and the means to meet this responsibility.

The President and Congress can give the Surgeons General full authority and ample means, but except by the draft neither the President nor Congress is able to give them a sufficient number of men from the medical profession, as it is a volunteer service. Consequently, if the Medical Departments are furnished with the authority and the means, they will still be unable to do their work unless the medical profession of the country, and particularly the younger men, respond more freely than they have done up to this time.

In the army hospitals and first aid work abroad, in the vast concentration camps so soon to be organized in this country, and in every branch of the naval service there is an urgent demand for each physician who can and will offer his services. In the work our country has pledged itself to do, the need for doctors is imperative. Estimates give the figure of 20,000

physicians as the minimum number necessary for this work. Only about 6000 are at present enrolled. These figures speak for themselves.

Commissions in the Medical Reserve Corps are accorded on the basis of First Lieutenant, Captain and Major, with respective salaries of \$2000, \$2400 and \$3000 a year. Applicants may apply directly to the various examining boards throughout the different states and complete all preliminary arrangements without reference to the Surgeon General's Office. The completed papers should be forwarded directly to the Surgeon General by the president of the examining board. A complete set of papers must contain the physical examination, report of the examiner as to mental, moral and physical qualifications, a personal history form filled out by the applicant and sworn to before a notary, and a certificate of state registration (except where this year's graduates have not had time to take their State Board examination). Two letters should also be sent certifying as to citizenship and moral qualifications, and, if of alien birth, a certificate of naturalization.

Further information may be obtained from the State and County Committees of National Defense, or directly from Surgeon General W. C. Gorgas, of the Army, or Surgeon General W. C. Braisted, of the Navy, Washington, D. C.

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THE EFFECTS OF SERUM THERAPY IN ACUTE LOBAR PNEUMONIA.

By ARTHUR BLOOMFIELD.

(From the Medical Clinic of The Johns Hopkins Hospital.)

Through the courtesy of the Rockefeller Hospital which has supplied us with Type I antipneumococcus serum,* it has been possible during the past winter to employ specific serum therapy in a series of cases of acute lobar pneumonia. Although the number is too small to allow definite conclusions

as to the efficacy of the serum as a life-saving measure, certain observations of interest were made which are herewith put on record. They comprise studies of (1) the course of the septiemia in treated cases, (2) the changes in the agglutinins of the patient's serum, and (3) the serum reactions of a dangerous or undesirable nature.

Eleven cases were studied. They were all instances of frank lobar pneumonia, in which the Type I pneumococcus

* Cole, R. I. New York Medical Journal, 1917, CV, 223. Arch. of Int. Medicine, 1914, XIV, 56.

was demonstrated in the sputum or blood. Nearly all the patients were colored laborers and came in with the disease well advanced—thus presenting conditions unfavorable to treatment. In addition to the serum, hydrotherapy, digitalis, and symptomatic measures were employed.

The pneumococcus was usually isolated from the sputum by mouse inoculation, and the type determined by agglutination with stock immune sera. The serum was warmed to body temperature and injected intravenously by gravity, at the rate of 2 to 4 c. c. a minute. A preliminary desensitizing dose of 1 to 5 c. c. was given subcutaneously or intravenously. Blood cultures were made before and after treatments, and samples of blood were drawn for the agglutination tests.

The results are presented in the following protocols:

CASE 1.—E. T. (Med. No. 37609), colored, aged 21. Admitted on about the 7th day of the disease with consolidation of the entire right lung. General condition good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Mar. 2	10.00 a.m.	Admitted to ward.
7th day	11.30 p.m.	1 c.c. subcutaneously.	0
Mar. 3	12.15 a.m.	100 c.c. intravenously.
8th day	4.30 p.m.	100 c.c. intravenously.	0

Clinical Course.—The patient was admitted on about the 7th day of a moderately severe pneumonia with consolidation of the right lung. On the 8th day 200 c. c. of serum were given with gradual fall of temperature and pulse to normal during the two following days. On the 11th day there was a secondary rise of temperature to 101° F. which continued for about six weeks, the signs in the lung slowly clearing during this time.

No serum reaction of any sort was observed.

CASE 2.—W. J. (Med. No. 37225), colored, aged 21. Admitted on about the 8th day with consolidation of the right upper and middle lobes. General condition good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.*			
				1:1	1:2	1:4	1:8
Jan. 29	9.00 p.m.	Admitted to ward.
Jan. 30	11.00 a.m.	1 c.c. subcutaneously.	0	+++	++	+	0
9th day	12.00 noon	100 c.c. intravenously.
	1.00 p.m.	+++	++	+	0
Jan. 31	12.15 a.m.	+++	++	+	0
10th day	1.00 a.m.	100 c.c. intravenously.	++++	+++	++	0
	2.00 a.m.	++++	+++	++	0
	9.00 p.m.	0	++++	+++	++	++
	10.00 p.m.	100 c.c. intravenously.
	11.00 p.m.	++++	+++	++	++

* 1:1 = Equal parts of serum and bacterial emulsion.
++++ = Complete agglutination. 0 = No agglutination.

Clinical Course.—The patient was admitted on about the 8th day of a mild pneumonia with consolidations of the right upper and middle lobes. During the next two days 300 c. c. of serum were given. Crisis took place on the 10th day and convalescence was uneventful.

No early or late reaction to serum was observed.

CASE 3.—M. S. (Med. No. 37423), white, aged 48. Admitted on 5th day of the disease with consolidation of the right upper lobe. General condition fairly good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Mar. 1	6.00 p.m.	Admitted to ward.
5th day
Mar. 2	11.50 p.m.	1 c.c. subcutaneously.	0
6th day
Mar. 3	12.30 a.m.	100 c.c. intravenously.	0
7th day	10.00 p.m.	100 c.c. intravenously.	0
Mar. 4	8.00 p.m.	100 c.c. intravenously.	0
8th day

Clinical Course.—The patient was admitted on the fifth day of a severe pneumonia with consolidation of the right upper lobe. Three injections of 100 c. c. each were given on the 7th and 8th days. Each injection was followed by a fall of temperature of several degrees with a subsequent rise a few hours later. The temperature and pulse became normal on the 9th day, and remained so except for slight post-critical rises. There was no spread of the pneumonic process in the lung.

Serum Reactions.—No immediate reaction followed any of the injections. On the 13th day—six days after the first injection—a large urticarial patch appeared. Two days later an intense generalized erythematous and urticarial eruption appeared and continued for five days. There were no other manifestations of serum sickness. Discharged well on the 27th day of the disease.

CASE 4.—F. S. (Med. No. 37698), colored, aged 18. Admitted on 4th day of the disease with consolidation of the right lower lobe. General condition good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Mar. 31	6.00 p.m.	Admitted to ward.
4th day
April 1	12.00 noon	5 c. c. intravenously.	0	0	0	0	0
5th day	1.00 p.m.	100 c.c. intravenously.
	2.00 p.m.	0	++++	++++	++++	0
April 2	5.00 p.m.	100 c.c. intravenously.	0
6th day	6.00 p.m.	++++	++++	++++	++++
April 3	3.00 p.m.	100 c.c. intravenously.	0
7th day	4.00 p.m.	++++	++++	++++	++++

Clinical Course.—The patient was admitted on the 4th day of a moderately severe pneumonia with consolidation of the right lower lobe. On the 5th day 100 c. c. of serum were given, the injection being followed by a sharp drop of temperature to normal with a subsequent rise. On the 6th day and on the 7th day 100 c. c. were given, after which the temperature fell and the symptoms cleared. From the 7th to the 20th days there was low fever with occasional sharp rises. With one of these on the 15th day there was a profuse crop of urticarial wheals, which recurred for about a week. On the 16th day there were severe pains in the joints. This serum reaction, in summary, lasted from the 13th to the 20th day. From the 20th to the 24th day the temperature was normal and the patient seemed perfectly well. On the 24th day there was a sudden rise of temperature to 103° F., high fever persisting for three days and then falling critically. During this period there were urticaria, joint pains, and adenitis.

Uneventful convalescence without further complications.

CASE 5.—L. G. (Med. No. 37611), colored, aged 24. Admitted on the 3d day of the disease with consolidation of the left upper lobe. General condition good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Mar. 24	6.00 p.m.	Admitted to ward.
Mar. 25 4th day	1.30 p.m.	1 c. c. subcutaneously.	0
	2.30 p.m.	100 c. c. intravenously.	0

Clinical Course.—The patient was admitted on the 3d day of a moderately severe pneumonia with consolidation of the left upper lobe. On the 4th day 100 c. c. of serum were given. No more serum was given on account of the reaction following the first dose. The course of the disease seemed to be uninfluenced by the serum, lysis occurring during the 7th, 8th and 9th days. Daily blood-cultures were all sterile, and there was no spread of the pneumonic process to other lobes.

Serum Reactions.—There was no reaction to the desensitizing dose of 1 c. c. The intravenous dose of 100 c. c. was followed in a few minutes by a fulminating immediate reaction. There was extreme cyanosis and dyspnœa; the chest was filled with rales, the patient frothed at the mouth, the pulse was extremely rapid and feeble; there were nausea, vomiting, and loss of sphincter control. This reaction was controlled to some extent by adrenalin and atropin, but one hour after the start there was a profuse general urticaria which persisted for about 24 hours.

From the 9th to the 15th day the temperature was practically normal and the patient felt well. On the 11th day there was a transient urticaria; on the 15th day a sharp rise of fever to 103° F., high, irregular fever persisting for five days, when it fell by crisis. During this period the leucocytes rose from 8000 to 24,000 with 6 per cent eosinophiles, and there were intense persistent pains in the joints and muscles without objective change. There was no adenitis and no urticaria, or urinary changes. The pains and fever cleared critically after five days and convalescence was uneventful. No septic complication was made out.

CASE 6.—W. R. (Med. No. 36946), colored, aged 29. Admitted on the 5th day of the disease with consolidation of the right lower and middle lobes. The patient was semi-conscious and seemed desperately ill.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Dec. 28 5th day	2.00 p.m.	Admitted to ward.
	7.00 p.m.	1 c. c. subcutaneously.	900	++	0	0	0
	7.45 p.m.	100 c. c. intravenously.
	8.15 p.m.	++++	0	0	0
	12.00 m.	25	++++	0	0	0
Dec. 29 6th day	12.15 a.m.	200 c. c. intravenously.
	1.00 a.m.	++++	++	0	0
	11.15 a.m.	50	+	0	0	0
	11.30 a.m.	100 c. c. intravenously.
	12.00 noon	++++	++++	0	0
	2.00 p.m.	Died.

Serum Reactions.—Within one-half hour after the first injection there was a slight chill. No apparent reaction after other injections.

The serum exercised no noticeable effect on the patient's general condition. The temperature, pulse and respirations remained high. He died in sudden collapse.

During a period of 16 hours 400 c. c. of serum were given. There was a marked reduction of the number of colonies (from 900 per c. c. to 25 per c. c.), and a definite increase in the agglutinative titer of the patient's serum.

There was no apparent spread of the pulmonary involvement.

Autopsy.—Lobar pneumonia of the right lower and middle lobes. Fibrinous pleurisy, bronchopneumonia (left lower lobe).

CASE 7.—F. S. (Med. No. 36968), white, aged 34. Admitted on the 5th day of the disease with consolidation of the right lung.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Dec. 27	4.00 p.m.	Admitted to ward.
Dec. 28 6th day	12.00 m.	1 c. c. subcutaneously.	30	0	0	0	0
	12.40 a.m.	100 c. c. intravenously.
	1.10 a.m.	++	0	0	0
	11.30 a.m.	2	++++	++	0	0
	11.45 a.m.	100 c. c. intravenously.
	12.45 p.m.	++++	++++	++++	++++
	9.00 p.m.	+	0	0	0
	10.30 p.m.	100 c. c. intravenously.
	11.30 p.m.	++++	++	0	0
Dec. 29 7th day	11.30 a.m.	1	++++	++	0	0
	12.30 p.m.	100 c. c. intravenously.
	2.00 p.m.	++++	++	+	0
	7.30 p.m.	++++	++	0	0
	7.45 p.m.	100 c. c. intravenously.
	8.45 p.m.	++++	++	++	0
Dec. 30 8th day	10.30 a.m.	0	+++	++	0	0
	11.00 a.m.	100 c. c. intravenously.
	12.00 noon	0	++++	++++	++	0
	8.45 p.m.	0	0	0	0
	9.00 p.m.	100 c. c. intravenously.
Dec. 31 9th day	10.00 p.m.	0	0	0	0
Dec. 31 9th day	12.45 p.m.	0	0	0	0	0
	2.00 p.m.	Died.

Clinical Course.—The patient was admitted on the 5th day of a very severe pneumonia with consolidation of the right lower lobe. He was suffering from alcoholism, was in collapse and seemed desperately ill. During the next three days he received 700 c. c. of serum. There was no demonstrable effect on the clinical course—he continued to be delirious and desperately ill, dying in collapse on the 8th day. The temperature and pulse remained elevated. The pneumococci promptly disappeared from the blood following the injection of the serum, and did not return, but there was a spread throughout the right lung of the consolidation.

Following the first injection of serum there was a severe chill lasting about one hour. No reaction was noted after the other injections.

Autopsy.—Lobar pneumonia (right).

CASE 8.—H. R. (Med. No. 37477), white, aged 35. Admitted on the 7th day of the disease with consolidation of right lower lobe. The patient was delirious and seemed very ill.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Feb. 20 7th day	10.00 a.m.	Admitted to ward.
	8.00 p.m.	1 c. c. subcutaneously.	20	0	0	0	0
	10.00 p.m.	75 c. c. intravenously.
	11.00 p.m.	0	0	0	0
Feb. 21 8th day	1.00 p.m.	0	0	0	0	0
	2.00 p.m.	50 c. c. intravenously.
	3.00 p.m.	++	0	0	0
Feb. 22 9th day	3.00 p.m.	0	++	0	0	0
	4.00 p.m.	50 c. c. intravenously.
	5.00 p.m.	++++	++	0	0
Feb. 23 10th day	4.00 p.m.	0	++++	++	0	0
	5.00 p.m.	100 c. c. intravenously.
	6.00 p.m.	++++	++++	++	0

Clinical Course.—The patient was admitted on the 7th day of a severe lobar pneumonia. The right lower lobe was consolidated. The patient was suffering from alcoholism and was wildly delirious. During the first three days in the hospital 275 c. c. of serum were given. No sudden change in condition followed, lysis taking place during the 11th and 12th days. The blood-cultures became sterile after the first injection of serum, and after the third injection there was a definite increase in the agglutinative titer of the patient's serum. There was no spread of the lung involvement after the serum was given.

Serum Reactions.—The patient was restless throughout the first injection. When 70 c. c. had been given, he broke out into a sweat, which was followed in a few minutes by a profuse general urticaria. He suddenly became extremely cyanotic, there was marked asthmatic breathing, and the pulse, which had been about 120 to the minute, rose to 180. Examination of the chest showed typical asthmatic breath sounds and rales. About 10 minutes after the onset of the reaction, there was a violent chill lasting about half an hour. Following the administration of adrenalin, atropin, and morphin, the reaction gradually subsided, the rash persisting for about four hours.

The second injection of 50 c. c.—sixteen hours later—was followed in half an hour by a short period of wheezing, cyanosis and sweating. No chill and no rash.

The third injection of 50 c. c.—25 hours later—was not followed by any apparent reaction.

The fourth injection of 100 c. c.—25 hours later—was followed by a fulminating reaction exactly similar to the first one, but more severe, and lasting about four hours. The pulse at one time was over 200 to the minute, the cyanosis and dyspnœa were extreme and the patient seemed moribund.

No more serum was given, but during the next two days there was a lysis, the temperature reaching normal on the 15th day of the disease. During the following week there were occasional slight rises of temperature and slight transient urticarias. The patient became rational, and the signs in the lungs cleared. On February 28—the 15th day of the disease—he began to complain of pain in the left hip. On March 4—the 19th day—and 12 days after the first serum injection, the temperature suddenly rose to 103° F. with corresponding tachycardia, the high irregular fever continuing for a week. During this time there were intense joint pains, glandular enlargement, and crop after crop of urticarial wheals. No striking urinary changes were observed. The patient lost about 40 pounds in weight and was finally discharged well on the 50th day of the disease.

CASE 9.—C. W. (Med. No. 37584), white, aged 34. Admitted on the 4th day of the disease with consolidation of the right lung. Seemed very ill—irrational and cyanotic.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
April 2 4th day	12.00 m.	Admitted to ward.	1 in 10 c. c.
April 3	40
April 4 6th day	9.30 p.m. 10.30 p.m. 11.30 p.m.	5 c. c. intravenously. 125 c.c. intravenously.	40 0	0 ++++	0 ++++	0 ++++	0 ++
April 5 7th day	12.30 a.m. 1.30 a.m. 10.30 a.m. 11.30 a.m. 12.30 p.m.	125 c.c. intravenously. 100 c.c. intravenously. 100 c.c. intravenously. 0 +++++ +++++ +++++ +++++ +++++ +++++ +++++ +++++ ++++ +++++ 0 ++++
April 6 8th day	11.00 a.m. 12.00 noon 1.00 p.m. 11.00 p.m. 12.00 m. 100 c.c. intravenously. 100 c.c. intravenously.	0	+++++ +++++ +++++ +++++	+++++ +++++ +++++ +++++	++++ +++++ +++++ +++++	++ +++++ +++++ +++++
April 7 9th day	1.00 a.m. 3.30 p.m. 4.30 p.m. 5.30 p.m. 50 c.c. intravenously.	0	+++++ +++++ +++++ +++++	+++++ +++++ +++++ +++++	+++++ +++++ +++++ +++++	+++++ +++++ +++++ +++++
April 8	0
9	0
10	0
11	2
12	Optochin.	0
13	Optochin.	0
16	0
17	∞

Clinical Course.—The patient was admitted on the 4th day of a very severe pneumonia with consolidation of the right lung. Owing to delay in identification of the organism, treatment was not begun until the 6th day. During the next four days 700 c. c. of serum were given. Treatment was then discontinued owing to lack of serum. During the period of treatment there was marked increase in the agglutinative titer of the patient's serum, which fell during the next two days. The pneumococci could not be grown from the blood after the first injection of serum. The temperature and pulse were apparently unaffected, and remained markedly elevated until death on the 20th day of the disease. The last dose of serum was given on the 10th day. On the 14th day two colonies per cubic centimeter were obtained, daily blood-cultures having been negative until then. On the 15th and 16th days optochin was administered and the blood again became sterile. The blood cultures were all negative until the day of death when innumerable colonies were obtained. With the terminal sepsis were associated a purulent meningitis and arthritis and an acute endocarditis. There was no spread of the pulmonary process.

Serum Reactions.—Following the first injection there was a transient urticaria. No immediate reaction followed the other treatments. From the 13th to the 19th day there were severe joint pains, and on the 19th day a profuse urticaria.

Autopsy.—Lobar pneumonia, organizing (rt.), purulent arthritis (knee-joints), purulent cerebrospinal meningitis, purulent otitis media, acute vegetative mitral endocarditis.

CASE 10.—G. W. (Med. No. 37556), colored, aged 23 yrs.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Jan. 26	8.00 p.m. 9.00 p.m.	Admitted to Ward. 0
27	0
28	0
29	1 (Type II)
30	0
31	0
Feb. 3	0
4	0
5	0
6	1 (5 cc.) (Type I)
7	2 (Type I)
8	1 (Type I)
9	0
10	9.30 p.m. 10.30 p.m.	1 c.c. subcutaneously. 100 c.c. intravenously.	0	0	0	0
11	2.00 p.m. 2.45 p.m. 3.45 p.m. 100 c.c. intravenously.	0	0 0	0 0	0 0	0 0
12	11.00 a.m. 11.45 a.m. 12.45 p.m. 100 c.c. intravenously.	0	++++ +++++	0 +++++	0 0	0 0
13	1.00 p.m. 2.00 p.m. 3.00 p.m. 100 c.c. intravenously.	0	++++ +++++	++++ +++++	0 +++++	0 0

Clinical Course.—The patient was admitted on the 3d day of a moderately severe pneumonia with consolidation of the right lower lobe. A Type II pneumococcus was isolated from the sputum and later from the blood. On the 7th day there was a sharp drop of the temperature and pulse almost to normal. The blood-cultures became negative, and there were signs of resolution. On the 11th day there was a sharp rise of temperature to 105° F., and the

leucocytes rose from 15,000 to 45,000. At this time signs of consolidation appeared in the left upper lobe. Three days later a Type I pneumococcus was isolated from the blood. It seemed clear that there was a fresh pneumonia due to a Type I organism. Serum therapy was begun on the 7th (?) day of this infection, 400 c. c. being given during the next three days. The temperature and pulse-rate fell, reaching normal on the 10th day. Agglutinins could be demonstrated in the patient's serum during treatment, and the daily blood-cultures were sterile. There was no further spread of the consolidation, but there was delayed resolution lasting over a period of about one month, during which a moderate continuous fever persisted.

Serum Reactions.—No immediate reaction followed any of the four injections. On the 14th day—seven days after the first injection—generalized urticaria, adenitis, and stiff neck appeared, lasting about three days. On the 21st day the patient developed a localized phlegmon of the lower abdominal wall which cleared up after incision and drainage. Further convalescence was uneventful.

CASE 11.—C. J. (Med. No. 37503), colored, aged 28. Admitted on 4th day of the disease with consolidation of the entire right lung. General condition good.

Date.	Hour.	Serum.	Pneumo- cocci per c. c. of blood.	Agglutinins.			
				1:1	1:2	1:4	1:8
Jan. 27	2.00 p.m.	Admitted to ward.
Jan. 28 5th day	12.05 a.m.	1 c.c. subcutaneously.	0	++	0	0	0
	12.30 a.m.	100 c.c. intravenously.
	1.30 a.m.	+++	++	0	0
	1.00 p.m.	100 c.c. intravenously.	0	+++	++	0	0
	2.00 p.m.	++++	+++	++	0
Jan. 29 6th day	11.30 a.m.	++++	+++	++	0
	11.45 a.m.	100 c.c. intravenously.	0
	12.45 p.m.	++++	+++	++	++
Jan. 30 7th day	12.15 p.m.	++++	++++	+++	++
	12.30 p.m.	100 c.c. intravenously.	0
	1.30 p.m.	++++	++++	++++	++++
	12.45 a.m.	++++	++++	++++	++
Jan. 31 8th day	1.00 a.m.	100 c.c. intravenously.
	2.00 a.m.	++++	++++	++++	+++
	11.45 a.m.	++++	++++	++++	++
	12.00 noon	100 c.c. intravenously.	0
	1.00 p.m.	++++	++++	++++	++++
	10.00 p.m.	++++	++++	++++	++
	10.45 p.m.	100 c.c. intravenously.
Feb. 1 9th day	11.15 p.m.	++++	++++	++++	++++
	8.00 p.m.	++++	++++	++++	++
	9.00 p.m.	100 c.c. intravenously.	0
Feb. 2 10th day	10.00 p.m.	++++	++++	++++	++
	8.00 p.m.	++++	++++	++++	+++
	8.15 p.m.	100 c.c. intravenously.	0
Feb. 3*	9.15 p.m.	++++	++++	++++	++++
	0
	0
Feb. 4	0
	0
	0
Feb. 5† 13th day	11.00 a.m.	+++	++	0	0
	12.00 noon	100 c.c. intravenously.	0
	1.00 p.m.	+++	+++	++	++
Feb. 6 14th day	3.00 p.m.	+++	+++	++	0
	4.00 p.m.	100 c.c. intravenously.	0
	5.00 p.m.	++	0	0	0
Feb. 7	0
Feb. 8	0	0	0	0	0
Feb. 8-21	Daily	blood culture.....	0

* Gradual fall of temperature which practically reached normal February 3.
† February 5 sharp rise of temperature to 103°.

Clinical Course.—The patient was admitted on the 4th day of a moderately severe pneumonia with consolidation of the right lung. During the following six days he received 900 c. c. of serum. There was no demonstrable effect on the clinical course, the temperature falling by lysis during the 8th, 9th, and 10th days of the disease. On February 5, the 13th day of the disease and nine days after the first injection of serum, there was a sharp rise of

temperature to 103.5° F., but without evidence of spread of the pneumococcus infection. Injections of 100 c. c. of serum on February 5 and 6 were followed in about 10 minutes by a severe chill, dyspnoea and tachycardia, although there had been no reaction following any of the previous injections. The fever was unaffected and remained high for the following three weeks; it then fell gradually to normal over a period of a month. During this period the signs in the chest were those of slow resolution, and there was no further involvement (frequent X-ray control). The leucocytes ranged from 20,000 to 40,000. From February 6 to 12 there were severe abdominal pain and rigidity; from February 10 to March 12, intense continuous pains in joints, and aching and stiffness of entire body. On February 15 a marked general glandular enlargement appeared, which persisted for three weeks. The cervical glands varied in size up to 5 cm. in diameter. By March 15 the adenitis and joint pains had cleared up and the leucocytes had become normal. The temperature became normal at about this time. No urticaria or rash was seen at any time. The urine contained a small amount of albumin throughout, but no casts.

Discharged well, April 6, 1917.

DISCUSSION.

1. *The Effect of the Serum on the Presence of Pneumococci in the Blood.*—In five of the cases pneumococci were present in the blood (900, 20, 40, 30 and 2 colonies per cubic centimeter) before treatment was begun. In four of these the blood promptly became sterile after the injection of the serum, although in Case 9 there was a terminal sepsis after 14 days. In Case 6 the one injection reduced the colonies from 900 to 25 per cubic centimeter, but did not prevent death; in Case 4 the patient died without any reappearance of the organisms in the blood. In six cases no organisms were present on admission, and the blood remained sterile throughout. All these patients recovered.

The serum is, therefore, clearly an effective agent in sterilizing the blood, and in preventing the development of septicemia.

2. *The Changes in the Agglutinins in the Patient's Serum Following Treatment.*—The agglutinins were studied in eight of the cases. There was a striking variation in the titer of various patients' sera even after injection of the same amount of serum. Thus, in Case 9, agglutinins were present in considerable quantity after 125 c. c. of serum, whereas in Case 10 none could be demonstrated after 200 c. c. of serum. Furthermore, the titer of the patient's serum following therapy bore no constant relation to the outcome of the case. In Case 8, for example, the septicemia cleared up before agglutinins could be demonstrated, and the patient recovered from a very severe pneumonia with only a slight transient appearance of agglutinins in his serum. In Case 9, on the other hand, the patient, after having a high titer and sterile blood for 13 days, died with an overwhelming pneumococcus sepsis. The titer of the patient's serum is therefore no certain guide to the efficacy of treatment.

3. *The Effect of Serum-Therapy on the Clinical Course of the Disease.*—There was no striking change in the clinical course of the cases which could clearly be attributed to the serum. Crisis took place in Case 4 on the 7th day; the other cases cleared by lysis at about the normal time—between the 7th and 12th days. No striking critical falls of temperature

were observed after injections of serum, nor was there in any instance any sudden relief of symptoms. The total stay in the hospital was, however, much prolonged by the severe relapsing serum disease which occurred in most of the cases. It should be mentioned that many of the patients observed during this season presented marked elevations of temperature during convalescence with signs of slow resolution. This was so not only in Type I infections, but also in the other groups.

4. *The Serum Reactions.*—The following table summarizes the incidence of the serum reactions:

Case No.	Reaction immediately after serum.	Total serum.	Late reaction.
2	None.	300 c. c.	None.
1	None.	200 c. c.	None.
6	None.	400 c. c.	Died before incubation period had elapsed.
7	None.	700 c. c.	Died before incubation period had elapsed.
3	None.	300 c. c.	Slight.
10	None.	400 c. c.	Moderate.
4	None.	300 c. c.	Severe.
11	None.	1100 c. c.	Very severe.
9	Slight.	700 c. c.	Severe.
8	Fulminating.	275 c. c.	Severe.
5	Fulminating.	100 c. c.	Severe.

Without dwelling on the usual features of serum disease a few points of special interest may be noted. In two cases (about 20 per cent) very alarming reactions followed immediately after the initial injection, although no indication of hypersusceptibility had been furnished by the preliminary "desensitizing" dose. The patients presented the picture of

acute anaphylactic shock. In Case 8 two reactions of this nature occurred following the first and fourth treatments, the second and third being uneventful. In five cases (45 per cent) there were very severe late reactions. These were featured by long periods of high fever and prostration punctuated by various symptoms of serum disease. In the case of C. J., Case 11, who received 1100 c. c. of serum, a marked reaction persisted without intermission for 37 days, in Case 4 for 20 days, and in Case 8 for about 14 days.

5. *Complications.*—Apart from the serum reactions, no complications occurred in any of the cases except in Case 10. This patient developed an abscess of the abdominal wall. Resolution was delayed in Cases 1, 10 and 11.

6. *The Curative Value of the Serum.*—The present series throws little light on the curative value of the serum. Most of the patients were treated after the 5th day, so that abortive terminations of the disease, suggestive of effective therapy, could not be obtained. Furthermore, two of the three fatal cases were practically moribund when the serum was given. A case such as No. 8, however, clearly seems to have been saved by serum therapy. This patient was admitted on the 7th day with 20 colonies per cubic centimeter of blood and recovered promptly after treatment. In one case only, No. 7, did the pneumonic lesion spread after the serum had been administered.

A STUDY OF THE INCIDENCE OF THE TYPES OF PNEUMOCOCCI ISOLATED FROM ACUTE LOBAR PNEUMONIA AND OTHER INFECTIONS, AND AN ANALYSIS OF THE CASES CLASSIFIED BY TYPES IN REGARD TO MORTALITY, COMPLICATIONS, ASSOCIATED DISEASES, BACTERIEMIA, AND LEUCOCYTOSIS.

By MILDRED C. CLOUGH, M. D.

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Beginning with February, 1915, an attempt was made to determine the group of pneumococcus concerned in all cases of lobar pneumonia in adults occurring in the wards of the Johns Hopkins Hospital according to the classification of Dochez and Gillespie.¹ Through the kindness of Dr. Howland, of the Department of Pediatrics, 13 cases of lobar pneumonia and 14 cases of empyema in children were studied. In addition, pneumococci from cases of bronchopneumonia, chronic and acute bronchitis, meningitis, peritonitis, and infection in ears and sinuses were included in the work. I have studied the incidence of the different types of pneumococci isolated between February, 1915, and September, 1916, in these conditions, and have analyzed in detail the acute lobar pneumonias in adults, classified according to the group of pneumococcus concerned, as regards age, mortality, complications, bacteriemia and sepsis, leucocytosis, and the presence or absence of associated diseases.

The organisms were isolated by blood culture, cultures from washed sputa, mouse inoculations with sputum, and, in a

number of cases, from material obtained by lung puncture. In many of the cases several methods were used and the results compared. Pneumococci isolated by blood culture in cases with clinical lobar pneumonia were considered to be the type causing the pneumonia. In most cases cultures obtained by lung puncture were pure, though in one case pneumococci were associated with large numbers of influenza bacilli. Cultures from the lung direct at autopsy in this case showed influenza bacilli only, the pneumococci presumably having died out.

Pneumococci isolated from washed sputum cultured on blood agar plates, when obtained in pure culture, corresponded in all the 10 cases tested to the strains obtained by lung puncture or blood culture. In five cases cultures from the washed sputum showed pneumococci and influenza bacilli together in pure culture. In three of these cases material from lung punctures was obtained, and pneumococci alone were grown in pure culture from it. In these three cases the influenza bacilli doubtless came from the smaller bronchi, but were evidently not concerned in the disease process in the lung.

Pneumococci of Groups III and IV "fished" from sputum cultures that were not pure were not considered, without other evidence, necessarily to have any etiological relationship to the pneumonia. Several such strains acted like saprophytic mouth organisms, in that they were markedly phagocytatable even in heated normal serum. In one case a Group IV pneumococcus was isolated from the sputum, while the patient's serum caused agglutination and phagocytosis of Group II pneumococci so markedly as to leave no doubt but that the case was a pneumonia due to a Group II strain.² In one case of lobar pneumonia strains belonging to both Groups III and IV were isolated from the same sputum culture. In one case of bronchopneumonia pneumococci belonging to an Atypical Group II and Group III occurred in the same sputum culture. In another case of lobar pneumonia, a Group IV was isolated from the sputum and an Atypical II from the blood.

When the sputum was easily washed, cultures were preferred to mouse inoculations for several reasons. By culture the presence of *Bacillus influenzae* as the cause of an empyema (not included in this study) was demonstrated in one case, and *B. influenzae* associated with a Type IV pneumococcus in another case. The association of *Bacillus influenzae* with an Atypical Type II pneumococcus in the lung of a case of lobar pneumonia has already been mentioned. The influenza bacilli would not have been demonstrated in these cases by mouse inoculation. In the two cases mentioned before, in which a Group IV and an Atypical II pneumococcus were each associated with a Group III in the sputum culture, mouse inoculation would probably have resulted in a sepsis with the mucosus strain. In these cases the Group III was probably a mouth organism, and the Group IV the cause of the pneumonia, since both cases recovered after a very mild course. With the relatively avirulent Type IV and Atypical II strains, mouse inoculation was especially unsatisfactory. Often mice did not die even after the injection of relatively large amounts of sputum intraperitoneally, or they died with sepsis from some other organism. Material from lung punctures contained so few pneumococci, that it was insufficient to kill mice when injected intraperitoneally, even in the case of the more virulent strains.

Group determinations were made by testing the agglutinability of the organisms with sera I and II obtained from the Rockefeller Institute through the kindness of Dr. Cole. Group III strains were identified by their morphological and cultural characteristics. Organisms agglutinating slowly with Group II serum, and only in the more concentrated dilutions, 1-32 or under, at the end of 24 hours, were considered Atypical II strains. Several organisms agglutinating atypically with serum I, and several agglutinating with both sera are included under the heading miscellaneous. These are at present being studied in detail. Of the Atypical II strains, four (all from lobar pneumonias) belonged to Avery's Subgroup IIA, and five (three of which were from pneumonias, one from a maxillary sinusitis, and one from a meningitis) belonged to Subgroup IIB.³ The other strains were not classified in this way.

In all, 121 strains of pneumococci were isolated and the groups determined. Table 1 shows the incidence of the different groups in numbers and percentages in the various conditions studied.

TABLE 1.
INCIDENCE OF THE TYPES OF PNEUMOCOCCI IN THE VARIOUS DISEASES STUDIED.

	Total No.	Type I		Type II		Type III		Type IV		Type Atypical II		Misc.	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Lobar pneumonia—adults...	54	19	35.2	3	5.5	8	14.8	11	25.9	9	16.7	1	1.9
Lobar pneumonia—children.	13	4	30.8	1	7.7	0	0	4	30.8	3	23.1	1	7.7
Empyema—adults	6	2	33.3	0	0	1	16.7	2	33.3	1	16.7	0	0
Empyema—children	14	7	50	2	14.3	0	0	3	21.4	2	14.3	0	0
Bronchopneumonia	10	1	10	0	0	2	20	3	30	2	20	2	20
Chronic bronchitis	5	0	0	0	0	0	0	3	60	0	0	2	40
Acute bronchitis	2	0	0	0	0	0	0	1	50	1	50	0	0
Sinusitis, otitis media, etc...	13	1	7.7	0	0	2	15.4	8	61.5	2	15.4	0	0
Meningitis	3	0	0	0	0	0	0	1	33.3	2	66.6	0	0
Peritonitis	1	0	0	0	0	0	0	0	0	0	0	1	100
	121	34		6		13		39		22		7	

The following points are brought out in this table:

1. The percentage incidence of Groups I, III, and IV in the lobar pneumonias in adults corresponds very closely to figures obtained at the Rockefeller Institute in their pneumonias from 1912-1916 (Group I, 33.54 per cent; Group III, 11.18 per cent; Group IV, 23.64 per cent);⁴ and approximately to those obtained by Mathers⁵ in Chicago, by Walker⁶ in Boston, by Richardson⁷ and by Lewis⁸ in Philadelphia. The striking feature in this series is the relatively very low percentage of typical Group II pneumococci, and the correspondingly high percentage of Atypical Group II strains. Of these latter strains, three were classified by Avery³ as belonging to Subgroup IIA, and another was identified as a Subgroup IIA by means of serum sent from the Rockefeller Institute. Two other strains studied by Dr. Paul W. Clough² by means of phagocytic tests showed the reactions of Atypical Group II organisms. The remaining three strains were agglutinated by serum II at the end of 24 hours in dilutions of 1-4, 1-8, and 1-8, respectively, the controls in normal horse serum being negative. In the statistics hitherto published, Atypical Group II organisms have not been differentiated from typical Group II strains, except in the series for the year 1915-1916, reported by Stillman⁴ from the Rockefeller Hospital. Of 102 strains included in his report, Subgroup IIA occurred five times and IIX once, a total of about 6 per cent. This differentiation is probably important, since members of these subgroups usually have a relatively low virulence for animals, and since they have been isolated from the mouths of normal individuals.^{3,4} It is probable, therefore, that they will be shown epidemiologically to resemble Type IV rather than Types I and II.

2. The small series of lobar pneumonias in children showed a slightly lower incidence of Groups I and III, with a correspondingly higher incidence of Groups IV and Atypical II as

compared with the lobar pneumonias of adults. If, however, the empyemas in children are added to the pneumonias and the percentage of these sums calculated, the incidence of Groups I and II becomes slightly higher than in the pneumonias in adults. These figures do not correspond to those given by Pisek and Pease,⁹ Wollstein and Benson,¹⁰ and Mitchell,¹¹ who have found a higher percentage of pneumonias due to Group IV in children than in adults. This discrepancy may be explained in two ways. In the first place, only lung puncture material was used for the cultures in this series, while most of the cultures obtained by the other authors were from sputum. In this study Group IV pneumococci have several times been

centage incidence of the different groups in their lobar pneumonias only (excluding bronchopneumonias), the percentages obtained (Type I, 32 per cent; Type II, 39 per cent; Type III, 3 per cent; Type IV, 25 per cent) correspond very closely to those reported from the Rockefeller Hospital in their series of 313 cases of lobar pneumonia in adults from 1912-1916. (Type I, 33.5 per cent; Type II, 31.6 per cent; Type III, 11.1 per cent; Type IV, 23.6 per cent.⁴) Wollstein and Benson studied 11 cases of lobar pneumonia and 36 cases of bronchopneumonia. In their cases, also, the percentage incidence of the different types in the lobar pneumonias, if separated from the bronchopneumonias, is not very different from the figures

TABLE 2.
CHRONOLOGICAL INCIDENCE OF LOBAR PNEUMONIA IN ADULTS BY TYPE.

1915											
	February.	March.	April.	May.	June.	July.	August.	Sept.	October.	November.	December.
Type I.....				•							••
Type II....		•									
Type III...			•••						•	••	
Type IV....		•••	•	•						••	•••
Atypical Type II..	•	•	•••	•							

1916								
	January.	February.	March.	April.	May.	June.	July.	August.
Type I.....	•	•••	•••••	•••	•	•		•
Type II....	•			•				
Type III...			•				•	
Type IV....			••	•	•	•		
Atypical Type II..				••	•			

isolated from the sputum in pneumonias due to the fixed types, and Wollstein and Benson¹⁰ and others report similar experiences. The isolation of a Group IV pneumococcus from a mixed culture of sputum, or even by mouse inoculation with sputum, cannot, therefore, be considered as undoubted evidence that the pneumonia is due to a Group IV organism. In the second place, all the cases in the series were lobar pneumonias, while the authors mentioned included bronchopneumonias with lobar pneumonias in their statistics. Pisek and Pease⁹ studied 48 cases of pneumonia of both types and found 22.9 per cent due to Group I, 29.3 per cent due to Group II, 8.3 per cent due to Group III, and 39.8 per cent due to Group IV. Only 28 of these cases were lobar pneumonias, and of them nine were due to Group I, eleven to Group II, one to Group III, and seven to Group IV. If one calculates the per-

in adults. In all these reports the percentage of the bronchopneumonias in children due to Groups I and II is relatively very low. This was also the case in our study of the bronchopneumonias in adults, as is shown in Table I. It seems probable, therefore, that the incidence of the different types in children is approximately the same as in adults.

Of the Atypical Group II pneumococci isolated from lobar pneumonias in children and from empyemas, three out of the six belonged to Subgroup IIB. This is of some interest, because Stillman⁴ reports that of the six cases of pneumonia due to Atypical Group II at the Rockefeller Hospital, none was due to Subgroup IIB.

3. A Group I pneumococcus was isolated from one out of 10 cases of bronchopneumonia. The other cases were due to Types III, IV and Atypical II in about equal percentages. It is of interest that one of the Group III bronchopneumonias

died six months later from a Group III lobar pneumonia. Pneumococci from cases of acute and chronic bronchitis belonged in every case to either Group IV or Atypical Group II with the exception of two atypical pneumococci classified under miscellaneous.

4. An interesting case in which a Group I was isolated from an otitis media and from mouth sputum gave a history of a mild pneumonia following "grippe" nine months previously, and presumably had been a carrier throughout this period.

5. The meningitis cases studied belonged to the relatively avirulent Groups IV and Atypical II, one of the Atypical Type II strains belonging to Subgroup IIB.

Table 2 shows graphically the incidence of the different types in lobar pneumonia in adults by months from February, 1915, to August, 1916.

The almost total absence of pneumonias due to Group I during the year 1915 shown in Table 2 is striking, while in the spring of 1916 an epidemic of Group I pneumonias occurred. In April, 1915, three cases due to Group III were admitted to the hospital within three days, and in October and November there was another series of three cases. Except for the summer months, the Group IV cases seemed to be more evenly distributed throughout the year than were the fixed types. These facts, if borne out in a larger series, would support the view that Group IV infections may be autogenous, in contradistinction to the probably epidemic nature of pneumonias due to the fixed types.

Table 3 shows the incidence and mortality of the pneumonias in adults due to the different groups of pneumococci, with the average age of the cases; the percentage of cases with and without associated diseases; and the percentage mortality of the cases subdivided in this way.

TABLE 3.
THE RELATION OF THE TYPE OF PNEUMOCOCCUS IN LOBAR PNEUMONIA IN ADULTS TO MORTALITY, COMPLICATIONS, AGE, AND ASSOCIATED DISEASES.

Types.	In- cidence.		Mor- tality.		Compli- cations.		Aver- age Age.	Cases with associated diseases.				Cases without associated diseases.			
								In- cidence.		Mor- tality.		In- cidence.		Mor- tality.	
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	No.	%
I	19	35.2	7	36.8	6	31.6	32.5	5	26.3	3	60	14	73.7	4	28.5
II	3	5.5	0	0	1	33	27.6	1	33.3	0	0	2	66.6	0	0
III	8	14.8	8	100	4	50	45.3	2	25	2	100	6	75	6	100
IV	14	25.9	8	57.2	5	35.7	46.5	10	71.4	7	70	4	28.6	1	25
Atypical II	9	16.6	4	44.4	2	22	40.2	5	55.5	3	60	4	44.5	1	25
Misc.	1	2	0	0	0	0	53	0	0	0	0	1	100	0	0
Total....	54	100	27	50	18	33.3		23	42.6	15	65.2	31	57.4	12	38.7

As shown in the table, the total mortality of the series was high (50 per cent). All of the eight cases due to the pneumococcus mucosus died. The mortality of the Group IV cases was relatively very high (57.2 per cent), and much higher than that given by Cole²² for the Group IV pneumonias at the Rockefeller Hospital (16 per cent) and by Mathers⁵ in Chicago (25 per cent). The explanation for these results in our series is probably the greater average age of the cases of this group (46.5 years), and the very high percentage of asso-

ciated diseases in these cases (71.4 per cent), as compared with 26.3 per cent, 33.3 per cent, and 25 per cent in the fixed types. Marked alcoholism is included as an associated disease on account of the large part which it seems to play in the incidence and mortality of pneumonia. The same explanation is offered for the mortality of the pneumonias due to Atypical II strains, which is higher than one would expect with organisms which are usually relatively avirulent. Several terminal pneumonias and one post-operative pneumonia were included in this study, all of which were due to Type IV or Atypical II organisms.

The following is an enumeration of the associated diseases occurring in the pneumonias due to the different types:

GROUP I.

- 14 cases—none.
- 2 " alcoholism and latent syphilis (Wass. R. +). 41 and 38 years.
- 1 " latent syphilis (Wass. R. +), emphysema. 50 years.
- 1 " alcoholism. 23 years.
- 1 " chronic endocarditis. 30 years.

GROUP II.

- 2 cases—none.
- 1 " alcoholism, 30 years.

GROUP III.

- 6 cases—none.
- 1 " lymphatic leukemia. 30 years.
- 1 " syphilitic cirrhosis of liver. 62 years.

GROUP IV.

- 4 cases—none.
- 2 " alcoholism. 36 and 58 years.
- 1 " pulmonary tuberculosis, cystitis, hydronephrosis (?). 52 years.
- 1 " prostatic abscess, syphilitic periostitis, chronic pancreatitis. 55 years.
- 1 " alcoholism and latent syphilis (Wass. R. +). 45 years.
- 1 " alcoholism, cirrhosis of liver, syphilitic aortitis, arteriosclerosis. 49 years.
- 1 " chronic tuberculosis. 60 years.
- 1 " alcoholism, carcinoma of stomach with perforation and peritonitis, latent syphilis (Wass. R. +), chronic tuberculosis, arteriosclerosis. 57 years.
- 1 " alcoholism, hypertension, hemiplegia, mitral insufficiency, acute bacterial endocarditis (?). 61 years.
- 1 " pulmonary tuberculosis. 40 years.

ATYPICAL GROUP II.

- 3 cases—none.
- 1 " pregnancy. 28 years.
- 1 " post-operative (operation for prostatic hypertrophy). 65 years.
- 1 " alcoholism, chronic tuberculosis, bronchiectasis, chronic nephritis, chronic fibrous pleurisy and peritonitis, syphilitic aortitis. 43 years.
- 1 case alcoholism, tuberculosis. 17 years.
- 1 " alcoholism, diabetes with coma, arteriosclerosis, emphysema. 41 years.
- 1 " syphilis (Wass. R. +), emphysema, aneurism (?), syphilis of aorta (?), lung tumor (?). 58 years.

Group IV and Atypical II pneumococci, then, seem to be the most frequent cause of lobar pneumonia in old people, in those with chronic diseases, in terminal pneumonias, and in pneumonias occurring in alcoholics; and the high mortality of these two groups in our series is probably dependent upon the associated conditions. In all the types the mortality was much higher in those cases with associated diseases than in those without.

The complications aside from sepsis were more frequent in the pneumonias due to the fixed types, especially Type III, than in those due to Atypical II and IV types, while sepsis was a much more frequent complication in the latter two types, as is shown in the next table. The complications, excluding sepsis, met with in each group are as follows:

- GROUP I.

13 cases—none.
3 “ delayed resolution.
1 “ otitis media.
1 “ peritonitis.
1 “ pneumothorax following pleural aspiration.
- GROUP II.

2 cases—none.
1 “ pleural effusion (not purulent).
- GROUP III.

4 cases—none.
1 “ empyema.
1 “ pericarditis.
1 “ empyema and pericarditis.
1 “ acute bacterial endocarditis.
- GROUP IV.

10 cases—none.
1 “ pericarditis.
1 “ empyema.
1 “ acute bacterial endocarditis.
1 “ thrombosis.
- ATYPICAL GROUP II.

7 cases—none.
2 “ pericarditis.

Tables 4 and 5 show the percentage of positive blood cultures obtained in the lobar pneumonias in adults divided according to the types of pneumococci concerned, and the relation of the positive cultures to mortality.

TABLE 4. INCIDENCE OF BACTERIEMIA, AND ITS RELATION TO MORTALITY IN LOBAR PNEUMONIAS OF EACH TYPE.									
Types.	Number Cultured.	Cases with negative cultures.				Cases with positive cultures.			
		Incidence.		Mortality.		Incidence.		Mortality.	
		No.	%	No.	%	No.	%	No.	%
I	17	13	76.5	3	23.1	4	23.5	4	100
II	3	3	100	0	0	0	0	0	0
III	3	2	66.6	2	100	1	33.3	1	100
IV	11	6	54.5	2	33.3	5	45.5	4	80
Atypical II....	5	2	40	0	0	3	60	2	66
Total.....	39	26	66.6	7	26.9	13	33.3	11	84.6

TABLE 5. RELATIONSHIP OF BACTERIEMIA TO MORTALITY.					
	Incidence.	Cases with negative blood cultures.		Cases with positive blood cultures.	
		No.	%	No.	%
Cultured cases which died.....	18	7	38.9	11	61.1
Cultured cases which recovered	21	19	90.5	2*	9.5

* Both cases had only one colony per c.c. of blood.

The percentage of positive cultures in the whole series was somewhat lower (33.3 per cent) than that obtained by Dochez,¹³ Rosenow,¹⁴ Strouse and Clough,¹⁵ Mathers,⁵ and others. This was due in part to the fact that a blood culture was taken on admission to the hospital, and was usually not repeated unless some special indication for it arose. A relatively high percentage of positive cultures was obtained in the pneumonias due to Group IV and Atypical II (all Subgroup IIA). One of the cultures from a Group IV pneumonia contained many thousand colonies per cubic centimeter of blood, and one from a Subgroup IIA case 2000 colonies per cubic centimeter. The more virulent Group I strains caused a bacteriemia in only half as many cases. In one of these cases there were 200 colonies per cubic centimeter, and in the remaining cases five colonies or less per cubic centimeter of blood. All the meningitis cases studied belonged to Groups IV or Atypical II, and Wollstein¹⁰ reports two cases both due to a Group IV pneumococcus. These findings suggest that the avirulent strains are more likely to enter and multiply in the circulation than are the fixed types. This may be due in part to the fact that most of the patients in this group were elderly individuals with associated diseases, and hence might have a lowered resistance to a general infection. However, the series is too small to warrant any definite conclusions on this point.

The mortality of the cases with bacteriemia is much higher than that of the cases with negative blood cultures, 84.6 per cent of the cases with positive blood cultures dying, as against 26.9 per cent of those with negative blood cultures. The relationship is shown in a different way in Table 5, in which all the cases cultured are divided according to whether they died or recovered. Of those which died, 61.1 per cent had bacteriemia, while of those which recovered, only 9.5 per cent (two cases) had pneumococci in the blood, and each of these cases had only one colony per cubic centimeter.

White blood counts were made on all the cases, and the average counts in the different groups of adult pneumonias compared. The counts were also averaged in cases with positive and in those with negative blood cultures, and in cases which died and in those which recovered, and the results entered in Table 6 for comparison.

The most striking feature in this table is the relatively low leucocyte count in the Group III cases (11,800). The highest count obtained is used for the averages, which, in the Group III cases, was usually on admission, the count in most of these cases falling with the progress of the disease. The average counts for the other groups are very close, 23,000 to 27,000,

TABLE 6.
LEUCOCYTOSIS IN THE LOBAR PNEUMONIAS OF EACH TYPE AND ITS RELATIONSHIP TO BACTERIEMIA AND MORTALITY.

Types.	Average Leucocyte Count.				
	All cases.	Cases with positive blood cultures.	Cases with negative blood cultures.	Cases which died.	Cases which recovered.
I	24,100	25,200	22,400	24,500	22,200
II	27,300	27,300	27,300
III	11,800	8,000	10,500	11,800
IV	24,600	20,200	31,500	17,700	32,600
Atypical II....	22,800	17,300	18,500	19,200	25,600

though in the cases due to Groups IV and Atypical II there were more instances of a hyperleucocytosis of over 40,000.

The leucocyte count was higher in the cases due to Groups IV and Atypical II which recovered than in those which died, and higher in the cases of Group IV with negative blood cultures than in those with positive blood cultures. As regards the cases due to Group I, the average counts were practically the same in those cases with negative and with positive blood cultures, as well as in those recovering and those dying.

SUMMARY.

In this study the grouping of 121 strains of pneumococci from different diseases was determined, and the percentage incidence of the different groups in the various conditions calculated. The lobar pneumonias in adults were analyzed in detail in regard to the mortality, age, presence or absence of associated diseases, complications, bacteriemia, and leucocytosis. No definite conclusions can be drawn from so small a series, but certain points were brought out which would be significant if confirmed by a large series.

In isolating the pneumococci, lung puncture cultures, blood cultures, sputum cultures, and mouse inoculations with sputum were used. Sputum cultures were preferable to mouse inoculations when a specimen of sputum which could be thoroughly washed was obtainable.

The percentage incidence of the different types of pneumococci in acute lobar pneumonia in adults corresponded very closely to that reported elsewhere, except for the low percentage of Group II and the correspondingly high percentage of Atypical Group II strains.

The percentage incidence of the types in lobar pneumonias in children, excluding bronchopneumonias, was approximately the same as in adults.

In three cases, two of which were lobar pneumonias in children and one an empyema in an adult, Atypical Type II pneumococci belonging to Subgroup IIB were isolated.

Of the bronchopneumonias, only one was due to Type I, and none to Type II. Types III, IV, and Atypical II occurred in about equal percentages. In the cases of acute and chronic bronchitis, otitis media, and sinusitis, but one pneumococcus belonging to Type I was isolated. This was a strain grown from the pus of an otitis media and from the mouth sputum of a patient who had probably been a carrier for nine months.

Pneumonias due to Groups I and III occurred in epidemics, whereas those due to Group IV were more uniformly distributed throughout the year.

The total mortality of the pneumonias in adults was high (50 per cent). The mortality among the Group IV cases was very high (57.2 per cent), due in part to the greater age of the patients and the high percentage of associated diseases, including alcoholism, which occurred in this group. In all of the groups the mortality was higher in cases with associated diseases than in those without.

Complications, apart from sepsis, were more frequent in the pneumonias due to the fixed types.

Blood cultures were positive in 33.3 per cent of all cases cultured. The percentage of positive cultures and the number of colonies per cubic centimeter of blood were higher in the cases due to Group IV and Atypical II than in those due to the fixed types. In all the types the mortality was very high in the cases with bacteriemia, and low in those without bacteriemia.

The white blood cell count was low in pneumonias due to the pneumococcus mucosus, and usually fell as the disease progressed. In the cases due to Group IV and Atypical II strains, the count was higher in those recovering than in those dying; and in the Group IV cases, higher in those without bacteriemia than in those with bacteriemia. In the Group I pneumonias the counts averaged about the same in the cases which recovered as in those which died.

REFERENCES.

1. Dochez, A. R., and Gillespie, L. J.: A biologic classification of pneumococci by means of immunity reactions. J. Am. M. Ass., 1913, LXI, 727-730.

2. Clough, P. W.: Personal communication.

3. Avery, O. T.: A further study on the biologic classification of pneumococci. J. Exper. M., 1915, XXII, 804-819.

4. Stillman, E. G.: A contribution to the epidemiology of lobar pneumonia. J. Exper. M., 1916, XXIV, 651-670.

5. Mathers, G.: The varieties of pneumococci causing lobar pneumonia with especial reference to their biologic differences. J. Infec. Dis., 1915, XVII, 514-521.

6. Walker: Quoted by Mitchell, A. G., 11.

7. Richardson: Quoted by Mitchell, A. G., 11.

8. Lewis: Quoted by Cole, R. I. Pneumococcus infection and immunity. N. York M. J. (etc.), 1915, CI, 1-7.

9. Pisek, G. R., and Pease, M. C.: A preliminary report on pneumonia in children with special reference to its epidemiology. Am. J. M. Sc., 1916, CLI, 14.

10. Wollstein, M., and Benson, A. W.: Types of pneumococcus found in the pneumonias of infants and young children. Am. J. Dis. Child., 1916, XII, 254-265.

11. Mitchell, A. G.: The types of pneumococci in infants and children. Penn. M. J., 1916-17, XX, 343-345.

12. Cole, R. I.: The specific treatment of acute lobar pneumonia. *Ibid.*, 345-351.

13. Dochez, A. R.: Occurrence and virulence of pneumococci in the circulating blood during lobar pneumonia. J. Exper. M., 1912, XVI, 680-692.

14. Rosenow, E. C.: Studies in pneumonia and pneumococcus infections. J. Infect. Dis., 1904, I, 280-312.

15. The blood in lobar pneumonia, J. Am. M. Ass., 1905, XLIV, 871.

15. Strouse, S., and Clough, P. W.: Blood cultures in pneumonia. Bull. Johns Hopkins Hosp., 1910, XXI, 247-251.

AN EPIDEMIOLOGICAL STUDY OF LOBAR PNEUMONIA.

By VIRGIL P. W. SYDENSTRICKER and ALAN C. SUTTON.

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During the past 10 months 66 cases of pneumonia have been treated in the medical service of the Johns Hopkins Hospital. Relatively few of the patients entered the hospital as early as the first or second day. The average admission was between the fourth and fifth day. A few were not seen until the tenth day or even later. We were able to determine the type of pneumococcus concerned in 97 per cent of the cases. The organism was isolated by either blood or sputum cultures. Lung puncture was never resorted to.

The identification of the strains of pneumococci was carried out along the lines in use at the hospital of the Rockefeller Institute.^{1,2} All sera used either for agglutination tests or treatment were given to us by that institute.

The distribution of the cases among the various types is given in Table 1. Twenty-four cases are included in Type I. Some of these patients received serum treatment; others did not. The entire subject of the serum treatment of these cases is dealt with fully in Bloomfield's paper. No cases due to Type III, *Pneumococcus mucosus*, occurred in the series. A large percentage of our cases were in negroes, 52 in contrast to 14 in whites.

The mortality rates for the entire season are given in Table 2. The table shows the rates for each group as a whole, and subdivided between blacks and whites. It also contains the rates for the season regardless of group distribution. Percentages computed from such a small group of cases as this are of little real value and at times misleading. They are given here in order to facilitate their use in the compilation of a similar but much larger group, several years from now. Of the 20 patients that died, five succumbed in less than 24 hours after reaching the hospital. All of these had a severe septicæmia, except one who died immediately on reaching the hospital, before any cultures could be obtained. Two died after being in the hospital 15 days. The rest lived from two to six days, averaging three and a half days in the hospital.

Complications were encountered in six cases. All were associated with a severe septicæmia. Pneumococci were recovered from the local foci in all instances. The distribution was:

Meningitis	4 cases.
Purulent arthritis	3 cases.
Pericarditis	1 case.
Otitis media	1 case.

Almost half of our cases of pneumonia came from Sparrows Point, Maryland. During November and up to the middle of December the cases from there were without exception Type I infections. We feared they might be the forerunners of a

Type I epidemic. This, together with the fact that the incidence of severe pneumonias during the winter months is always very high there, led us to undertake the following epidemiological studies. We hoped to throw some light on the presence of healthy carriers in this community, and to see whether the proportion of the various strains carried in the mouths of the healthy men was different from that known to exist elsewhere.^{3,4} The carrying out of this work was made possible by the courtesy and coöperation of the officials of the Bethlehem Steel Company, and of Drs. Carmine and Merriam in the company's employ.

Sparrows Point is the home of the Maryland Division of the Bethlehem Steel Company. It is situated on the waterfront near the mouth of the Patapsco River, about 10 miles below Baltimore. The plant employs about 7000 men. Some have homes in Baltimore, but the majority live in the town which has grown up around the plant. About 2000 of the men are negroes. Half of these live in the company's shanties, in a section of the works called "Coke Oven Row." This group of shanties is shown in Fig. 1, which is reproduced from the company's map with their consent. The shanties are built 10 in a row. Each accommodates four men. The shanty is a small room 14 feet square, with four bunks, four lockers, a washstand and a stove. One building is used as a store, barber-shop and pool-room. This is a common meeting-place and usually crowded. Most of the men get their own meals, but there is a cook-shop which some of the men use.

Formerly all the shanties were frame buildings, the wall being a single thickness of board. Recently a group of 100 tile and concrete shanties has been added. The shanty group is situated directly on the shore, and is consequently exposed to all sorts of weather. The majority of our pneumonia cases came from this Coke Oven group. The view commonly held among the company's physicians is that pneumonia has always had a high incidence and been of a severe form among these men in the shanties.

The group seems to offer excellent opportunities for epidemiological studies. It is an isolated group of 1000 men living under almost identical conditions. They are in intimate contact with each other and with no one else. They crowd into the store or into each other's shanties. They frequently close the two small windows and door, and, in addition, try to pack the cracks between the boards with newspaper, especially in winter, to keep out the cold. They sleep sometimes with the stove lit, or, if too tired to start a fire, they sleep without it, often with too few blankets. Thus these men are exposed to

¹ Dochez, A. R., and Gillespie, L. J.: J. A. M. A., 1913, LXI, 727.

² Dochez, A. R., and Avery, O. T.: Jour. Exp. Med., 1915, XXI, 114.

³ Dochez, A. R., and Avery, O. T.: Jour. Exp. Med., 1915, XXII, 105.

⁴ Stillman, E. G.: Jour. Exp. Med., 1916, XXIV, 651.

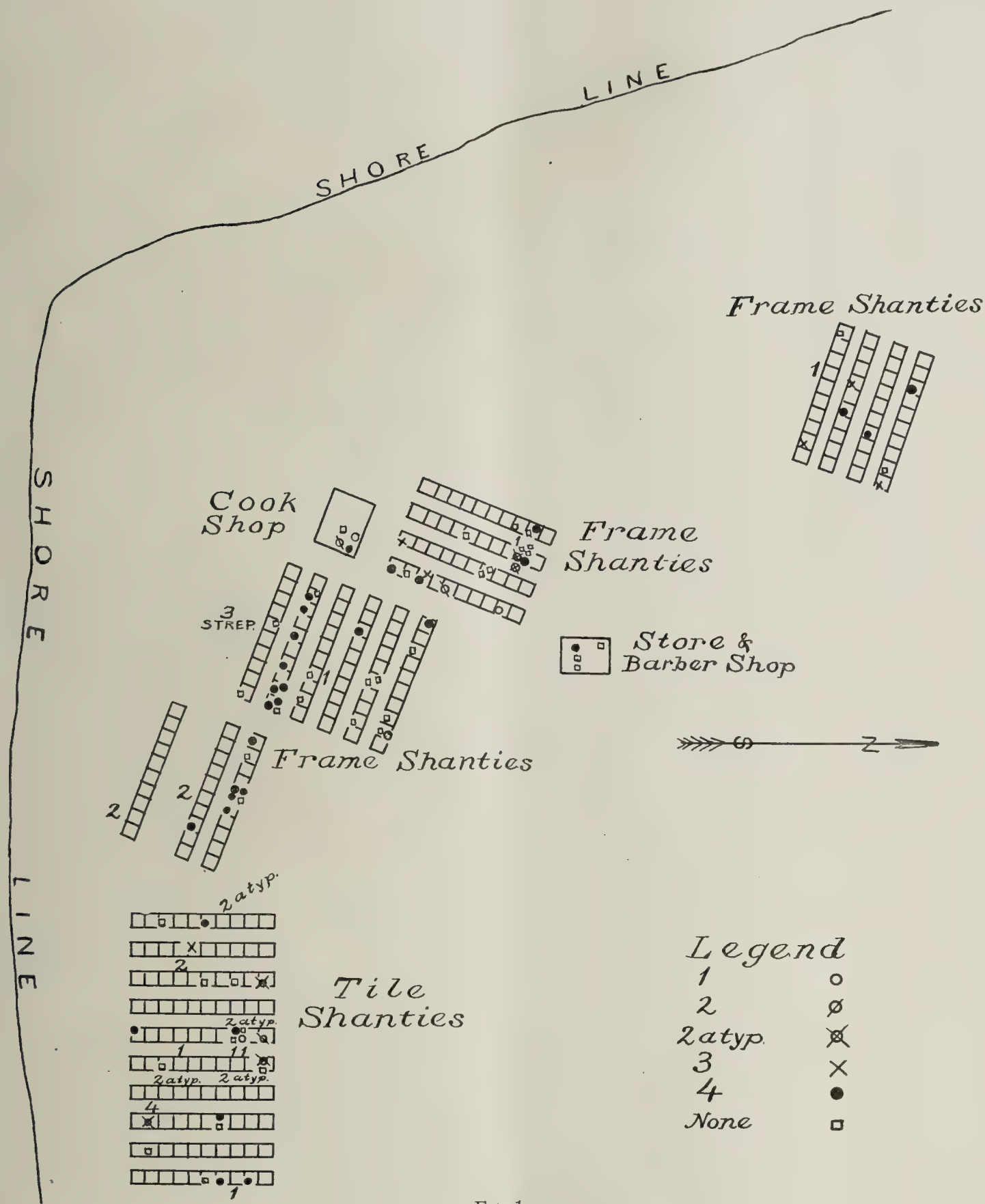


FIG. 1.

sudden changes of temperature. Few of them, however, are exposed to the heat of the furnaces, since practically all are employed on outside work. Another factor, which may play a rôle in their susceptibility, is that most of them come from the south and are not used to winters as severe as in this climate.

It is this group, then, that we undertook to study. We collected, during the latter part of January, specimens of sputum from 100 of these men. In Fig. 1 the types are spotted on their respective shanties. The figures by the shanties give the types of the cases of pneumonia from each shanty which were treated in the hospital.

Of the four men employed in the cook-shop, one carried a Type I, one a Type II, the other a Type IV, and one was free from pneumococci.

The sputa were collected in sterile bottles, brought immediately to the laboratory and white mice then inoculated with 0.5 c. c. of sputum subcutaneously. The mice were allowed to die and cultures made from the peritoneum and from the heart's blood. The pneumococci were usually obtained in pure culture.

In order to have a normal group with which to compare them, we cultured in a similar way 50 sputa collected at random among our dispensary patients. The results of these studies are tabulated in Table 3. The striking difference is in the high incidence of the fixed types in the Coke Oven group—the number of Type IV pneumococci is practically the same, the difference being in the small number of negative cultures in the Sparrows Point group. The high incidence of fixed types among the mouth organisms parallels the high percentage of fixed-type pneumonias and the extremely low percentage of cases due to the Type IV pneumococcus among Coke Oven Row cases, as contrasted with our city cases of pneumonia in Table 4. Another point is a pneumonia morbidity rate at Coke Oven Row of approximately 6 per cent, which is very high in comparison with the Health Department rate for Baltimore City of less than 0.5 per cent. The latter is an estimate based on the Health Department mortality rate. The mortality of the Sparrows Point group is shown in Table 5. It varies little from the rates given for the entire group.

Several interesting features warrant special mention. In Shanty 609 we collected sputa from six men. Two contained Atypical Type II pneumococci, one a Type IV, and three yielded no pneumococci. One of the last group later developed a Type I pneumonia. In Shanty 43 all four men developed pneumonia the same day, following a sudden fall in temperature. One was treated in another hospital in this city. The type of pneumococcus was not determined in this case. One refused hospital care and went to his home in the south. The other two came here. They had Type I and Atypical Type II infections, respectively. They stayed together in a side room by themselves the entire time. The one that was recovering from the Atypical Type II infection suddenly relapsed after his temperature had become normal. A lobe, in the opposite lung from the one previously involved, became consolidated. His blood cultures again became positive. This

time a Type I pneumococcus was isolated. Prior to the isolation of the Type I organism, the development in the patient's serum of antibodies active toward the Atypical II strain suggested that we would find that the new consolidation was due to a pneumococcus of an entirely different strain. This patient received antipneumococcus (Type I) serum and made an uneventful recovery except for a moderate serum sickness. If he contracted the Type I infection from his shanty-mate in the hospital, it is interesting that he contracted a different type in the shanty.

Summary.—Examination of 100 specimens of sputum from healthy negroes living in the shanties of the Bethlehem Steel Works showed 22 per cent of pneumococci belonging to fixed types in contrast to 6 per cent of a group of our dispensary patients. The number of the ordinary saprophytic Type IV organisms was practically identical in the two groups. The increase in the fixed types was at the expense of the group that does not harbor pneumococci in their mouths. This high percentage of healthy individuals carrying pneumococci of fixed types in their mouths occurred in a community where the percentage of cases of lobar pneumonia due to organisms of fixed types was likewise very high.

TABLE 1.
SUMMARY OF CASES.

Type.	Black.		White.		Total.
	Living.	Dead.	Living.	Dead.	
I	12	6	3	3	24
II	3	0	1	0	4
II (atypical)	7	4	0	1	12
IV	15	2	3	2	22
Ungrouped	1	1	0	0	2
Streptococcus mucosus ..	1	0	0	0	1
Friedländer's bacillus ...	0	0	0	1	1
Total	39	13	7	7	66

TABLE 2.
MORTALITY RATES.

Type.	Black. Per cent.	White. Per cent.	Mixed. Per cent.	
I	33 $\frac{1}{3}$	50	41.7	
II	0	0	0	} 31.3
II (atypical)	36.3	100	41.6	
IV	11.8	40	18.2	
Mixed	25	50	30.3	

TABLE 3.
PNEUMOCOCCI ISOLATED FROM MOUTHS OF HEALTHY INDIVIDUALS.

Type.	Sparrows Point (100 Cases). Per cent.	Dispensary (50 Cases). Per cent.
I	6	0
II	6	2
II (atypical)	4	2
III	6	2
IV	35	32
None	43	62
	100	100

TABLE 4.				
PNEUMOCOCCI ISOLATED FROM CASES OF LOBAR PNEUMONIA.				
Type.	Sparrows Point.		Baltimore City.	
	Number of Cases.	Per cent.	Number of Cases.	Per cent.
I	15	55.6	9	25.7
II	1	3.7	3	8.6
II (atypical) .	8	29.6	4	11.4
III	0	0	0	0
IV	3	11.1	19	54.3
	—	—	—	—
	27	100.0	35	100.0

TABLE 5.			
MORTALITY OF SPARROWS POINT GROUP.			
Type.	Number of Cases.		Mortality Rate. Per cent.
	Living.	Dead.	
I	12	3	25
II	1	0	0
II (atypical)	5	3	37.5
IV	2	1	50.0
	—	—	—
	20	7	35.0

A STUDY OF THE BACTERIÆMIA IN LOBAR PNEUMONIA.

By ALAN C. SUTTON and CHARLES E. SEVIER.

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In this, as in most laboratories, it has for some time been the custom to do a blood culture upon admission in all cases of lobar pneumonia, and to identify, if possible, the type of organism responsible for the infection. In case the blood culture should be negative, the group determination is made with the organism recovered by culture or mouse inoculation from the sputum—a less certain method. Consequently, more than one blood culture was rarely made on each patient, unless some unusual feature of the clinical course suggested the need for further investigation. Records were not made in all cases of the degree of the bacteriæmia.

This year we undertook to make a daily blood culture in every case of pneumonia from the day of admission until the temperature (rectal) was below 100° F. This was carried out in all except the first seven patients of the season, who had blood cultures taken only on admission, all of which were negative. There was one other patient who died immediately on reaching the hospital before a culture was obtained. So far as we know, there is no similar study reported on a group of cases in which the strains of the pneumococci were also determined.¹

We wished to determine the course of the sepsis in cases with positive blood cultures, to see whether this varied according to the type of infecting organism, and finally to determine the relation of the bacteriæmia to prognosis.

The method used in making the blood cultures is the usual one. A 10 c. c. Record syringe is used. First, 1 c. c. of a 1.5 per cent sodium citrate solution is drawn into the syringe. Then the syringe is filled to the 10 c. c. mark with blood. The blood and citrate are thoroughly mixed. Eight cubic centimeters of the mixture are plated with glucose-agar—in four plates. The remaining 2 c. c. are put into a flask containing glucose broth. Thus by using known amounts of blood and accurate dilutions the number of colonies per cubic centimeter can be determined. In cases with a severe sepsis much higher dilutions of blood are made. In these cases we use freshly made blood-agar instead of glucose-agar for plating.

The detailed results of the study are given in a set of tables. Each table shows all the cases in the series belonging to its particular strain. In Fig. 1 are shown all the cases due to the Type I pneumococcus. Only those cases with one or more positive blood cultures are represented graphically. The others, in which the organism was obtained only from the sputum, are tabulated merely in regard to the number of living and dead. Dots connected by solid lines represent the patients who died; rings are used for those who recovered. Broken connecting lines instead of solid ones are used during the period when the patients with a Type I infection received specific treatment with antipneumococcus serum furnished us by the hospital of the Rockefeller Institute. Lines of plus marks represent the period during which optochin was given. This was used in only two cases.

Of the 10 patients with positive cultures, only four recovered. Three of these had less than six colonies per cubic centimeter, and showed organisms at most on three days, one of them only once. The other, who received serum treatment, came into the hospital on the seventh day of the disease with 20 colonies per cubic centimeter. He received the first dose of 75 c. c. of serum on the day of admission and subsequent cultures were persistently negative. Of the six fatal cases, two of the patients died on the day of admission; one lived three days, showing an increasing bacteriæmia; the other three received serum treatment, which was followed by a reduction in the number of colonies per cubic centimeter in spite of the fatal termination.

None of the four cases due to the typical Type II organism had positive blood cultures.

The group of cases due to pneumococci that agglutinated atypically with Type II serum is given separately in Fig. 3. Of the 12 cases included under this head, seven gave positive cultures. Three of these had only one colony or less per cubic centimeter on from one to three days. Two had been negative on admission. The other came in on the third day, and his blood was positive only on the day of admission, showing only one colony in 3 c. c. of blood. All three recovered without complications. The four that died had marked grades

¹ Dochez, A. R.: Jour. Exp. Med., 1912, XVI, 680.

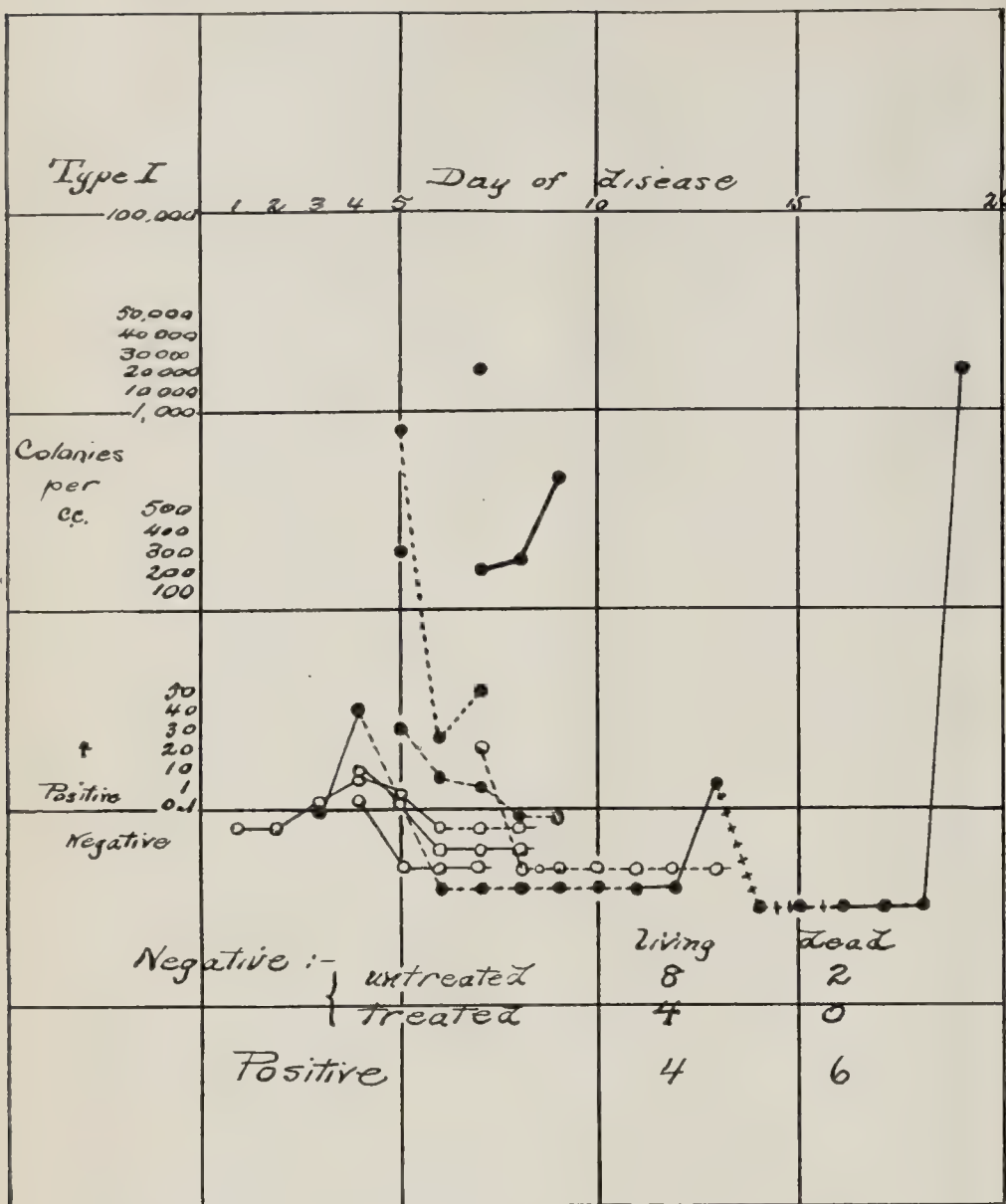


FIG. 1.

For figures 1 to 5:

Dots = Fatal cases.

Rings = Cases that recovered.

----- = Period of administration of Type I antipneumococcus serum.

++++ = Period of administration of optochin.

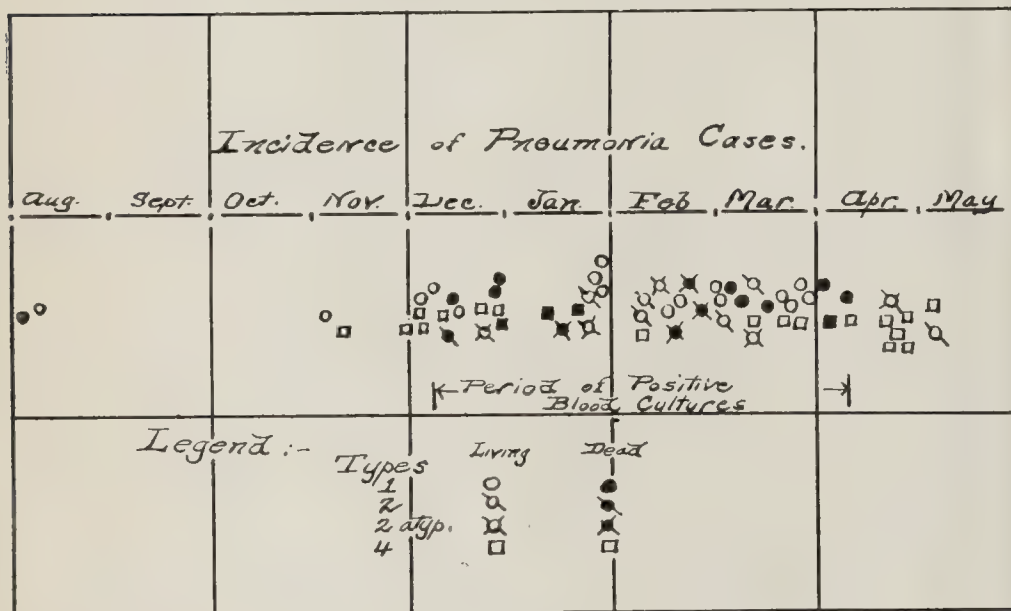


FIG. 6.

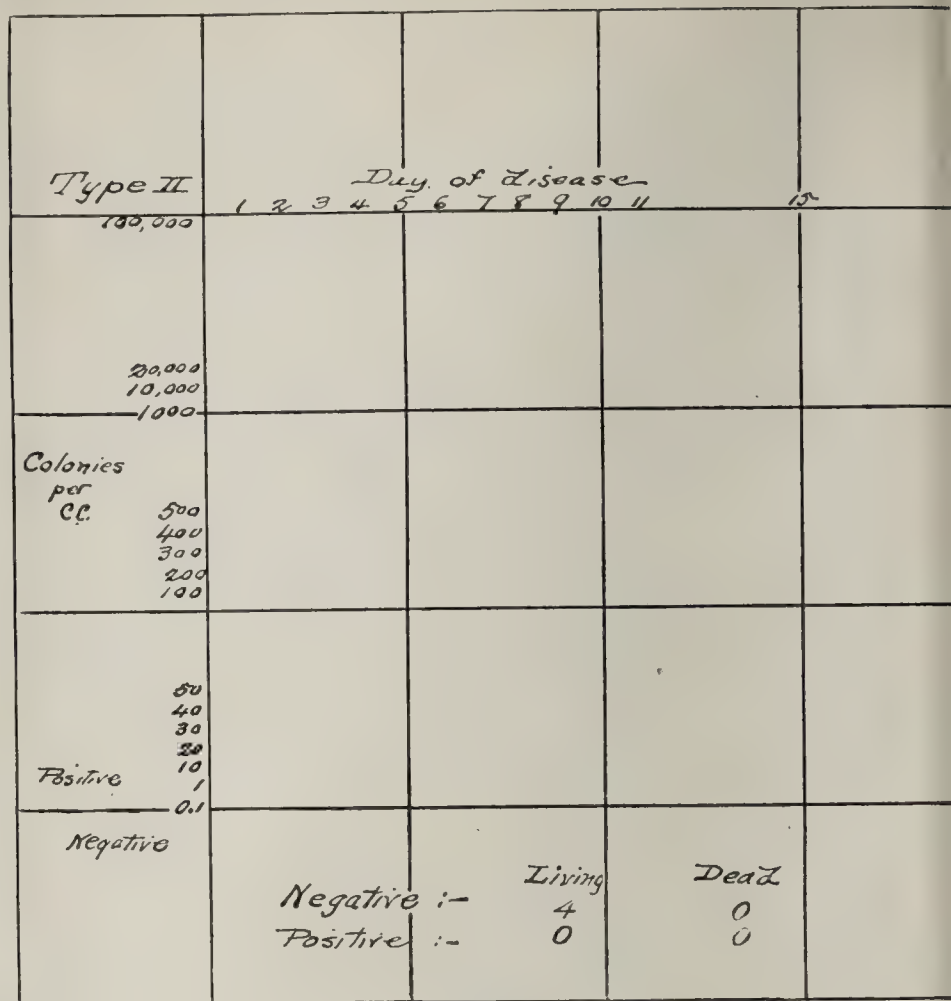


FIG. 2.

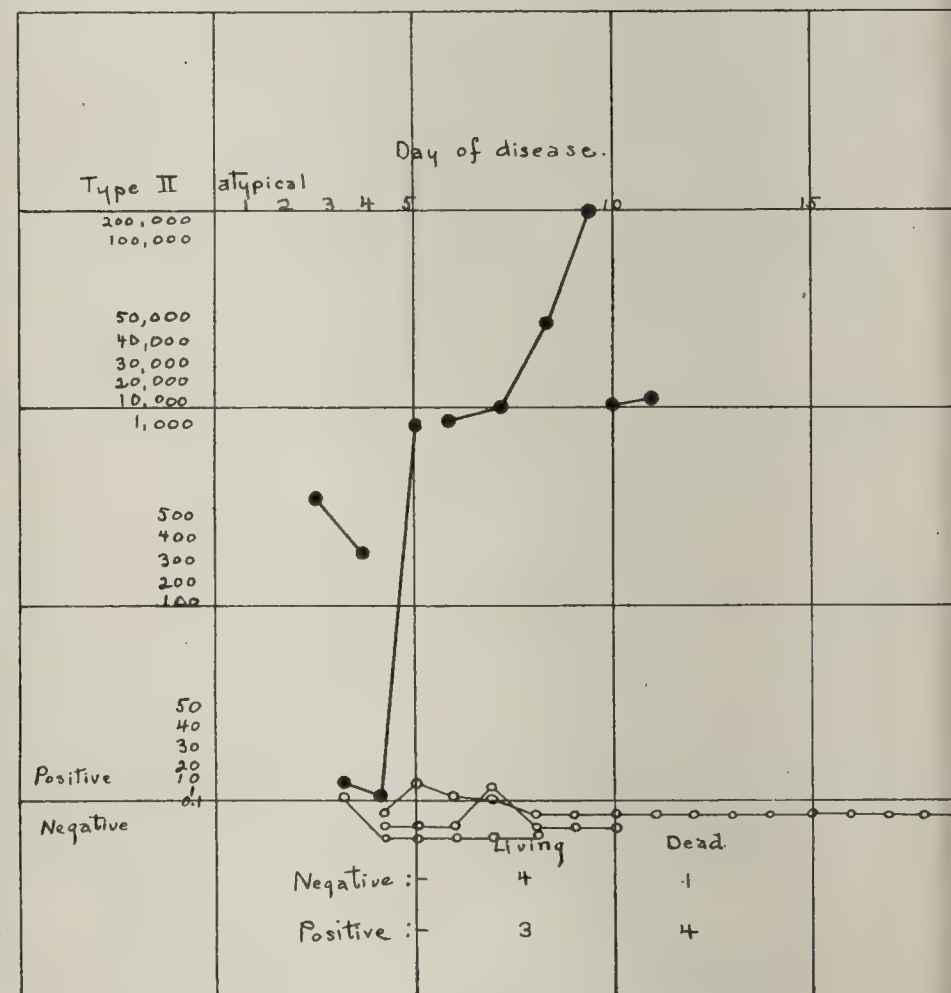


FIG. 3.

of bacteraemia. One patient came into the hospital on the tenth day of the disease with a severe septicæmia and meningitis. He died the following day. The patient who entered on the third day with five colonies per cubic centimeter, which on the following day had dropped to less than one colony per cubic centimeter, suddenly developed within 24 hours a bacteraemia of 1000 colonies per cubic centimeter and died. Autopsy revealed no complications whatever.

The cases not included under any of the fixed strains and commonly grouped as Type IV are shown in Fig. 4. They fall

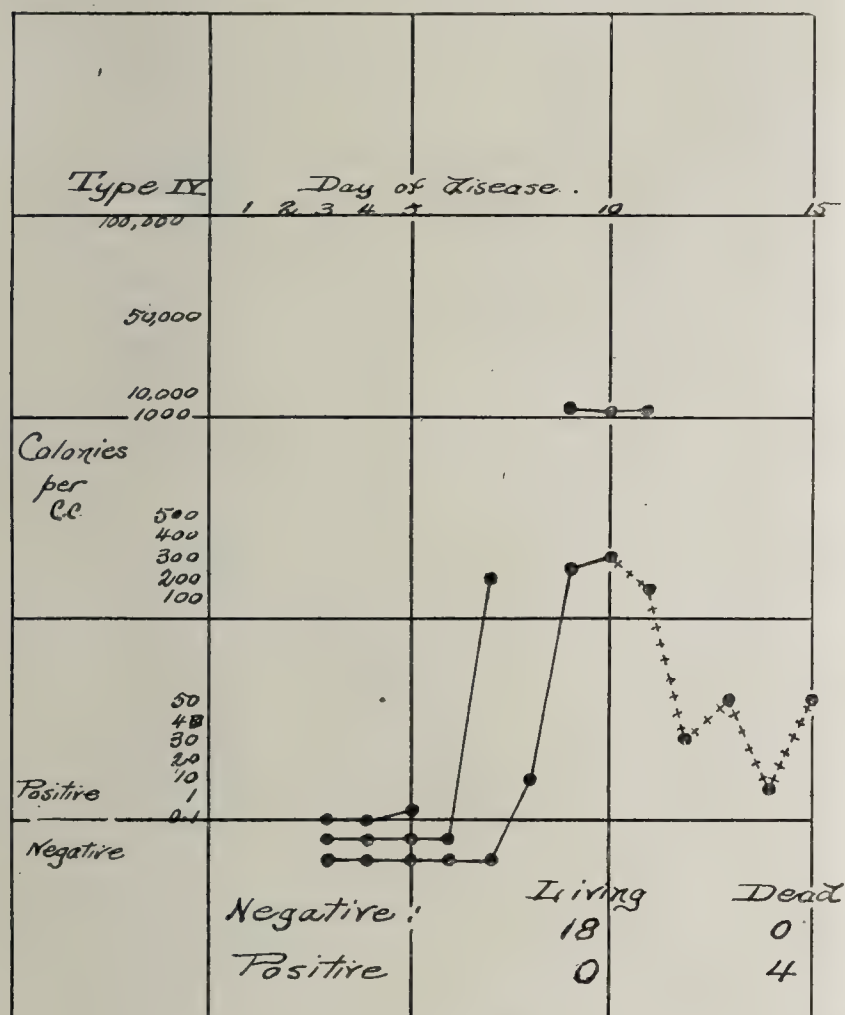


FIG. 4.

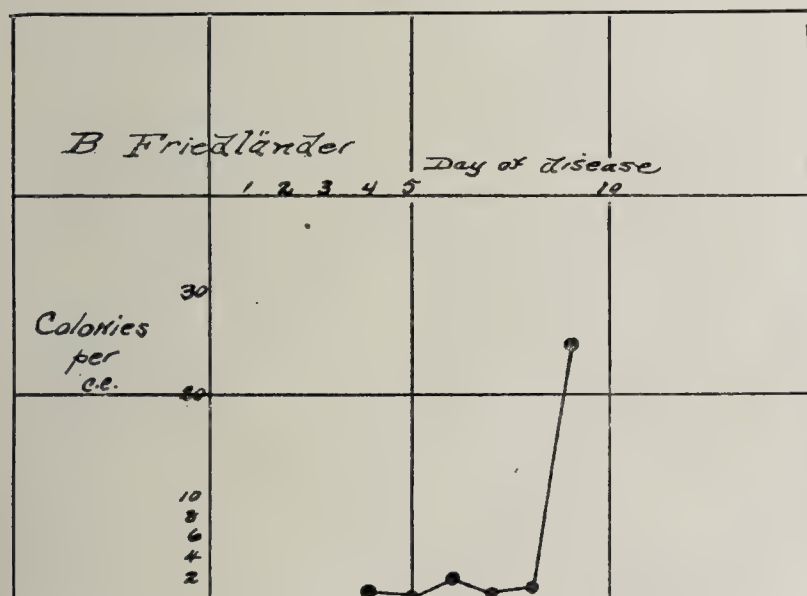


FIG. 5.

into two clean-cut groups: all the patients with positive blood cultures died; all with negative cultures recovered. The only case that showed a decrease in the grade of the bacteraemia received optochin therapy. The optochin was not started until the tenth day; the decrease in colonies was coincident with its use.

We had two cases of lobar pneumonia not included in the above groups. One is a case due to Friedländer's bacillus (*B. mucosus capsulatus*). The organism was isolated from the sputum and the blood. The course of the sepsis is given in Fig. 5. The patient was a white man, 52 years old, who came into the hospital on the fourth day of the disease and died on the ninth day.

The other case was caused by *Streptococcus mucosus*. It was agglutinated only by Type III serum, but was insoluble in bile and morphologically was not a Type III organism. The organism was not isolated from the blood. It was, however, gotten from the sputum in practically pure culture, twice by direct culture and once by mouse inoculation. That the organism was the one causing the pneumonia we feel is borne out by the fact that it was agglutinated by the patient's serum and not by normal sera.

From an analysis of all the cases the striking feature is the practical coincidence of the mortality percentage with the percentage of positive blood cultures. Consequently, the reason that the mortality rate of Type IV is low, while in some of the fixed types it is high, may easily be that the incidence of positive cultures is low, while in the fixed types it is high. The factors which determine whether a lobar pneumonia will run its course without bacteraemia, with only an occasional organism in the blood, or will develop a severe septicæmia, are probably complex. The virulence of the particular strain is probably by far the largest factor, but does not seem to be the only one. Our highest bacteraemia was noted in the case of a negro who came into the hospital on the sixth day of the disease. On admission he had 2000 colonies per cubic centimeter of blood. He lived four days with a rapidly increasing septicæmia that reached 180,000 colonies per cubic centimeter just before he died. The only complication was a purulent effusion in the right elbow-joint the day before death. The organism from this case was an Atypical Type II pneumococcus. Three weeks earlier we had a patient from the same locality, also with an Atypical Type II infection, who never had over one colony per cubic centimeter, and finally recovered after a long-delayed resolution. The organism isolated from the blood of the man who died was also agglutinated by the serum from the convalescent case.

Of the entire series of 66 cases only three patients died whose blood cultures were persistently negative. We secured autopsies on all three patients. Two died with massive lesions. In one of these all the lobes except the right middle were consolidated; in the other all but the right upper. In each case there was considerable amount of œdema of the uninvolved lobe. There were no complications. The patients died on the

sixth and eight days of the disease, respectively. In the third case the exact cause of death is obscure. The case stands alone in the entire series. The patient was a negro, 28 years of age. He had always been healthy. There was no evidence or history of anything more than a moderate use of alcohol. He entered the hospital on the third day of his illness, lived six days longer and then died. He had consolidation of the right upper and middle lobes only. There were no complications. Blood cultures were persistently negative. The case was one of Type I infection, but the patient did not receive serum treatment. He seemed no sicker than other patients with negative cultures before the crisis. His temperature ranged from 103° to 105° F. There was a leucocytosis varying between 20,000 and 25,000. His pulse was of good quality until the last day. He died in collapse, apparently exhausted by the so-called "toxemia."

Of the entire series no patient recovered who had, at any time of the disease, over five colonies per cubic centimeter of blood, whether he received specific therapy or not, with the exception of one patient who had 20 colonies per cubic centimeter on admission, and a severe alcoholic delirium. This patient, however, received serum within a few hours of admission, and subsequent doses until after his temperature had become normal.

Summary.—In Fig. 6 is shown the distribution of the cases throughout the year. The striking feature is that all the deaths, excepting that of the patient showing a negative blood culture, which is discussed separately, occurred in the four months between December 8 and April 8, although 16 cases occurred before or after this period. This is also the period within which all the positive blood cultures were obtained. Do the fixed types vary in virulence throughout the year, or does

the severity of the initial exposure during the period of maximal changes in weather predispose to the type of pneumonia that runs its course with a septicæmia?

The results of the series are summarized in Table 1. In general, the incidence of septicæmia runs parallel with the mortality. If the cases with a transient sepsis, having only an occasional colony early in the disease, are omitted, the percentages of positive blood cultures and mortality are practically identical.

The fatal cases fell into three groups:

- 1st. The patients dying with a septicæmia. This group included all but three cases.
- 2d. The two patients dying with almost complete consolidation of both lungs.
- 3d. The single patient dying apparently "of toxemia," with negative blood cultures and only moderate consolidation.

Finally, as regards prognosis, we have found blood cultures the most valuable aid. Ninety-three per cent of our patients with persistently negative blood cultures recovered without any complications. Of the patients with positive cultures, all with over five colonies per cubic centimeter at any period of the disease died, except one with 20 colonies on admission, who received serum therapy.

TABLE 1.

Types.	Percentage of positive blood cultures.	Mortality percentage.
I	45.8	41.7
II	0	0
II (atypical)	58.3	41.6
IV	18.2	18.2
	43.8	31.3

ON THE MECHANISM OF CONVULSIVE PHENOMENA AND ALLIED SYMPTOMS.*

By C. MACFIE CAMPBELL, M. D.

It is difficult in medicine to escape the narcotic influence of names and to keep alive a healthy curiosity as to the facts of experience and their interrelation.

Names, like the ideas of Plato, impose on us as objective entities outside of the individual facts. So in dealing with convulsive and allied phenomena, it is not easy to free oneself from the baleful influence of the words epilepsy and hysteria, and to think in terms of the modes of reaction of living organisms. It is, however, when we succeed in the effort to think in such terms that we are most likely to do justice to the individual case.

I propose, therefore, to discuss a few cases in such terms, not in the hope of throwing any light on nosological entities, but to see whether the symptoms can be made more or less intelligible.

To illustrate the point of view, one may take a symptom like headache and study the various settings in which it occurs. In some cases headache is adequately explained on a toxic basis, *e. g.*, the headache of kidney disease; at an equally simple level we can discuss the headache of brain tumor. In other cases the headache arises in the setting of an emotional reaction, and in emotion we deal with a more complex functional unit than is involved in discussing toxins and elimination, tissue anomalies and intracranial pressure.

In the case of other headaches we have to pass beyond the simpler conceptions of instinct and emotion and have to introduce associative material; the headache may become intelligible only when we consider those organized forces or trends that are grouped together under the conception of the subconscious, or whatever term may prove more acceptable to the purist. Still other headaches are woven into the conscious adaptation of the individual to his tasks, and help us to escape

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importunate visitors or to evade distasteful tasks, although with twinges of conscience.

To endeavor to find one simple formula suitable for all headaches would be a vain task; the symptom may be determined at any one of several levels, the ascending levels of organic integration.

The situation is further complicated by the fact that the symptom may be determined in the same case by factors at more than one level. Megrin headache, about which so little is known, may be assumed to arise at a simple level and not to require explanation in terms of the more complex factors of the personality; but in the case of the migrainous daughter of a migrainous mother, where the daughter has many repressed and poorly digested instinctive problems, who can apportion correctly the respective rôles of simple pathological physiology, of subconscious forces and of conscious adaptation?

The same problem meets us in relation to many other nervous symptoms, such as bed-wetting, night-terrors, choreiform movements, stammering. The latest achievements in psychopathology have shown us how complex may be the determination of even a simple symptom like bed-wetting. A young man of 18 had an isolated incident of bed-wetting after his father had urged him to make a public appearance from which he shrank; to understand the symptom it was necessary to descend to the roots of the personality. While such facts have to be recognized, one is entitled to protest against the formulation based on such a case being generalized, and applied to other cases which may be adequately formulated in terms of injudicious fluid intake, poor training, physiological inadequacy or simple emotional disturbance.

In relation to night-terrors, I see no reason to assume that this symptom must always involve reference to the most complex adaptive mechanisms, and may not sometimes arise at a much simpler level. I am well aware that night-terrors may be of most complex origin, that they may indicate tension in the most highly organized trends of the individual, and may spring from a blend of desire and aversion in relation to the fundamental instincts. The counterpart of night-terrors of such origin is to be seen in the waking life in the attitude towards something at once desired and dreaded, the anticipation of a mystery at once fascinating and terrible. All this may very well be true, and yet in other cases the symptom may arise at a much simpler level, and may require no reference to the complex elaboration of instinctive forces.

Choreiform movements in some cases are considered to be purely toxic manifestations (Sydenham's chorea), but similar symptoms may arise in the absence of toxic factors, as an adaptive mechanism by means of which repressed forces express themselves in a permissible disguise. Where a hysterical child, with a previous attack of Sydenham's chorea, seems to have a relapse, it is impossible to disentangle completely the rôle played by the impersonal factors from that played by the more complex determinants of human behavior.

With these facts in mind, one comes to the study of convulsive and associated phenomena with an open mind, willing to receive help from the most detailed chemical or histo-

pathological studies as well as from the most detailed psychopathological researches, such as the recent work of Dr. Pierce Clark, and not disposed to see any opposition between the two lines of study. One will neither deny the value of psychopathological interpretations because some cases seem to be adequately explained on more elementary principles, nor will one employ psychopathological explanations as general formulæ applicable in all cases.

In a graduated series of convulsions or allied phenomena, ranging from those of simple to those of complex determination, the convulsions of uræmia and general paralysis would represent one end of the scale; at the other extreme would be cases in which the attacks have to be expressed in terms of adaptive activity with conscious and subconscious determinants.

The latter group may be illustrated by the case of a young man * of 21, a farmer, who was brought to the hospital owing to a series of convulsions during the previous three days; he had been subject to attacks for several years. In the brief stay in the hospital he had several attacks, during which he thrashed around wildly and for which he professed complete amnesia; he also claimed amnesia for two episodes of elaborate pantomime which occurred in the hospital. On the fourth day after admission he was impatient to leave the hospital and said that he could control the attacks at will; that they had been developed in order to relieve him from uncongenial work. The reason why this method of evasion had been chosen was because these attacks came very easily; he had between the age of 6 to 14 lived near an epileptic boy and had frequently imitated his fits. Such was the explanation given by the patient.

It would, however, be rather crude to accept this formulation as an adequate analysis of the whole situation. The fact that in boyhood he had reacted to the fits of his comrade by imitating them shows a peculiar responsiveness to a rather dramatic situation, a tendency to identify himself with the hero of the mysterious sickness, a facile translation of the phantasied activity into real movements on his own part, an absence of inhibition by those restraining forces which are the most valuable elements in personality.

The patient's statement that he imitated the other boy's fits meant no more than that the more or less automatic dramatization of the attacks was unchecked by trends of a higher level, but was in harmony with the conscious directing forces of the personality, *e. g.*, love of prestige.

The earlier episodes in imitation of the epileptic boy and the later episodes under the stress of uncongenial work were not to be understood in the light of some abstract fiat of the will, but as the expression of a special organization of the instinctive and affective life of the patient. It may even be debated whether such a constitution does not include a special facility or explosiveness of motor discharge, and whether the

* This case was the subject of a communication made by Dr. J. E. Eidson before a joint meeting of the Washington Psychiatric Society and the Maryland Psychiatric Society of Baltimore, March 28, 1917.

patient did not imitate the convulsions of the epileptic boy because of his constitutional kinship to the latter; there is much truth in the French dictum that one only simulates what one has. The patient was self-willed, superficial, unduly ambitious, with an extremely violent temper; his memory had somewhat deteriorated.

The analysis of such a case, in terms of the different levels at which the symptoms are determined, offers more than does its exclusive reference to one of a series of diagnostic alternatives—malingering, hysteria, epilepsy.

In the following case there was no indication of the collaboration of the official personality in the development of the attacks.

The patient, a lad of 18, like the former patient, was a farmer, to whom his work was uncongenial. At 13 he began to be nervous, shaky, and subject to palpitation; at 17 one day he had a brief episode of faintness and dizziness; next day he fell unconscious, but did not have any jerking or loss of sphincter control. During the following year he was subject to attacks of weakness and dizziness with shortness of breath and palpitation. In the hospital there was noted only slight enlargement of the heart, slight respiratory irregularity of the pulse, a pulse rate of 90 to 100 per minute, and profuse sweating of the hands and feet. When venapuncture was performed, the patient became pale and lost consciousness; there were slight convulsive movements of the legs and arms, and of the jaw; a large amount of gas and a small amount of feces were passed involuntarily. The whole episode lasted about one minute, and in half an hour he was in his usual condition.

Three weeks later when lumbar puncture was attempted the patient complained of feeling faint, had a slight general convulsion of less than a minute's duration; there was no loss of sphincter control. The pulse dropped to 39 per minute, the skin was cold and pale. The patient claimed to have been conscious but unable to talk during the attack.

Lumbar puncture next day was followed by headache and vomiting. On the following day the patient had an attack lasting half an hour; the movements suggested those of coitus, the attack finished with a long sigh and general relaxation, but there was no erection nor emission. He could not be roused during the attack and had no memory for what transpired during the attack.

In this case determinants at the conscious level were not elicited; the attacks were to be considered either as the expression of factors at the subconscious level, or the expression of an idiosyncrasy of emotional reaction at the physiological level, or of a combination of these two factors. The rôle of subconscious sexual phantasies, strongly suggested by the last attack, may also have been important in the two earlier attacks, the reaction to the insertion of a needle.

It is, however, premature to assume that in all cases of fainting on trivial operations or at the sight of blood, the main determinants are subconscious phantasies; we must allow the possibility of individual idiosyncrasies of emotional reaction. The general nervousness of the patient from the age of 13 and

the earlier attacks of dizziness and weakness may have been determined neither at the instinctive nor at the subconscious level, but at the same level as the irregularity of the heart, and the profuse sweating.

According as one emphasizes the physiological idiosyncrasy on the one hand, or the rôle of repressed trends on the other, the case will be referred to epilepsy or to hysteria. As a matter of fact, the case is only adequately grasped when justice is done to both mechanisms. Can the discredited term hysterio-epilepsy not be used in a perfectly honest and definite way?

The following three cases illustrate more clearly the rôle played by the elementary physiological and emotional idiosyncrasy, while more complicated adaptive mechanisms are not in evidence.

A boy, seven and a half years of age, rather restless, with an irritating cough, given to violent tantrums, was subject to pain in the epigastrium on rising, and on his return from school. The pain was liable to appear under the stress of emotion. "If he gets frightened these pains come on him right away and make him pale and sick." One day he cut his finger, whereupon he fell on the floor, foamed at the mouth and kicked. On the following morning without known cause he had a similar attack. During the following year he has had no further episode; the irritating cough has disappeared.

A boy of 10, somewhat spoiled and irritable, on arising in the morning would be extremely pale and complain of malaise. He slept badly and had little appetite. On three occasions he fainted, the first time when he was vaccinated; the third time was at the age of nine during a physiology lesson at school. On the last occasion he was said to have been unconscious for over an hour. In the course of frequent interviews no psychogenic factors were apparent; careful examination of the heart disclosed no lesion, and improvement of his condition soon followed a healthy regime.

A girl of eight for several years had been subject to attacks of convulsive twitching, usually nocturnal; in the first attack she was apparently unconscious. One day she was bitten by a cat; when her father told her that she should suck the poison out of such a wound she became unconscious; her face and hands twitched. No psychogenic factors were elicited; the patient was a serious and conscientious child, somewhat reserved, subject to outbreaks of temper, rather dreamy, not much interested in her school work.

While in the two young farmers discontented with their work the symptoms seemed to require reference to the complex mechanisms of adaptation, in each of these three last cases we see one particular weak spot: In the first, epigastric pain is prominent; in the second, a vasomotor anomaly; in the third, muscular twitching; in each we see an idiosyncrasy in emotional reaction.

For the formulation of these cases physiological categories and those of the simple instinctive and emotional life may perhaps be sufficient.

An extremely important question is that of the rôle which these more fundamental disorders will play in the later adjustment of the individual. Will they be modified by good regime

and sound training, or will they become more deeply rooted through poor regime and habit and emancipate themselves completely from the control of the personality, conscious or subconscious; or will they be the handmaids of the subconscious and go halfway to meet its demands? So far as I know, at the present time these questions cannot be answered on the basis of clinical experience.

The emancipation from personal control of a motor reaction may be seen in the tic, or motor habit, which starting in the beginning as an adaptive act, subject to personal control, finally becomes independent and compulsive. The transition from the purposefully controlled to the independent and emancipated reaction may even be followed in such a complex type of reaction as the catatonic syndrome; this was the case in a patient accused of murder, who immediately after an interview with his lawyer developed a catatonic syndrome, which on later examination was found to have emancipated itself from the control of the personality (personal communication from Dr. Wm. L. Russell).

The same point of view may be illustrated by a second series of cases, presenting one symptom in common, namely, that of sudden and overpowering somnolence.

A young man of 19 complained of being frequently overcome with sleep even during conversation or walking. He attributed the condition to the fact that from the age of 14 he had deliberately cultivated the habit of falling asleep during tedious study hours. After a few months' practice he had become such an adept that he had merely to put his head down on the desk in order to fall asleep. He continued to indulge in this habit, but for more than a year previous to his admission to the hospital the habit had emancipated itself from his control; during reading, if he thought of sleep, he would drop off to sleep for an hour or so; the thought of the awkwardness of an attack during a conversation brought on sleep immediately. On one occasion he several times fell asleep at the wheel of his automobile and narrowly escaped disaster. In walking he would have brief spells of sleep and almost fall. The patient showed excellent physical health; there was no evidence of dyspituitarism.

The patient's explanation that the condition was merely the result of a habit is obviously inadequate. The sleep habit is not so easily cultivated and depends to a large extent on personal idiosyncrasy. For sleep to have been so successfully cultivated until finally it emancipated itself entirely from the patient's control, a very marked individual idiosyncrasy must be postulated. Deeper affective roots of the disorder or any special adaptive values were not to be traced; it did not seem to have anything in common with the prolonged sleep of some depressions, nor with the defensive mechanism of stuporous conditions. One was entitled to assume that what appeared to be the product of voluntary habit formation was in major part due to latent constitutional idiosyncrasy; just as the artificial convulsions of the young farmer were not altogether to be credited to his higher level mechanisms.

That the sleep mechanism may have a certain independence is shown by Gélinau's case,¹ where there was no question of

deliberate cultivation, but where the symptom developed, at least at the beginning, in an emotional setting. The patient, a cooper of 36, found that, if he laughed heartily or contemplated a profitable piece of business, his muscles would become limp and he would fall asleep for a minute or so. Later the condition developed to such an extent that he would fall asleep several times during a meal. Although the observation does not include an intensive study of the personality and of possible undercurrents, it suggests the possibility of a more or less special type of reaction not of an adaptive nature, but based on a personal idiosyncrasy, at first elicited in relation to the emotional life. Further studies may demonstrate the adaptive nature of this reaction and may trace it to its subconscious and instinctive roots, but we are not entitled to assume that special subconscious factors are concerned in its production.

Reference may also be made to Löwenfeld's case,² a boy of 17, who from the age of 13 showed a pronounced tendency to fall asleep suddenly at very frequent intervals. This seriously interfered with his school work, and later with his work in a factory. If he laughed, his muscles would relax, he would stagger, his knees gave way, he had to hang on to some support, he was liable to drop objects.

The imperative onset of sleep and the peculiar relaxation of the motor apparatus during laughter are interesting in view of the relation of the attacks of sleep in Gélinau's case to pleasurable excitement.

In cases like the following there is still less suggestion of the symptom being other than a deep-rooted constitutional anomaly, unexplained by any special associative material. The patient, a Polish boy of 15, had at the age of six and again at the age of nine been subject to spells in which he would sit down and fall asleep. At the age of 15 the spells returned; the patient would suddenly appear to fall asleep, and would sink upon a chair or fall to the floor. The eyelids would contract convulsively for a few minutes, the teeth be clenched, but the tongue was never bitten. There were no clonic or tonic movements of the limbs. The boy would seem to sleep for about 25 minutes and then would wake up. The patient was of very limited intelligence and had been unable to get beyond the third grade.

In this case the attacks had neither been encouraged by the boy, nor had they appeared in any special emotional setting; they seemed to have no relation to the complex factors that make up the personality, but to be related to the lower levels of the patient's reactive mechanism.

SUMMARY.

The review of cases of convulsive and allied phenomena discourages the application of a general formula to all cases, or the distribution of the cases among a limited number of nosological entities, hysteria, epilepsy, psychasthenia, etc. In each case the problem is: How far can we deal adequately with the symptoms in merely physiological terms, how far must we take into consideration the instinctive and emotional patterns of reaction, to what extent are the complex factors of the sub-

conscious and the conscious life involved in the development of the symptoms?

Where the symptoms occur in early life the prognosis must be made after a careful estimate of all the reactive assets of the individual, and not merely on the basis of statistical probabilities. The treatment must be directed not merely to the demonstrable or hypothetical physiological anomalies, but must take into consideration the formation of habits, the regulation and assimilation of the instinctive and emotional life, the forces involved in the interplay between the subconscious and conscious realms.

Perhaps some symptoms which on statistical grounds are far from encouraging may be modified by good regime and wise training, a fair environment and sound mental hygiene, and may disappear instead of becoming fixed through habit and emancipating themselves from the controlling forces of the personality.

REFERENCES.

1. Gélinau: Sur la narcolepsie. Gaz. des hôp., 1880, p. 626.
2. Loewenfeld, L.: Ueber Narkolepsie. Münch. med. Wchnschr., 1902, S. 1041.

THE FASCIOLOPSINÆ OF CHINA: A STUDY OF TWO SPECIES FROM CHEKIANG PROVINCE.

By N. WORTH BROWN, M. D.

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On the Eastern coast of China, particularly in the Province of Chekiang, are districts in which large numbers of the population harbor intestinal parasites identical with, or closely allied to, *Fasciolopsis buski*. These parasites have been frequently reported by medical missionaries and port physicians. Specimens have been sent to this country and to Europe for identification, descriptions of which conform to the general type discovered in 1843 by Busk, described by Lankester in 1857, and later by Looss (1899), Stiles (1901) and Odhner (1902). Ward in 1909 described three species from this section of China, recognizing *F. buski* and *F. rathouisi* (Poirier, 1887) and distinguishing from them another for which he proposed the name *F. goddardi*. In 1909 Rodenwaldt described an intestinal fluke from Egypt, *F. fülleborni*, which very closely resembles *F. buski*. From South China, from Cochin-China, from India and from Natal, specimens of *F. buski* have also been reported.

The material upon which the following report is based was secured from the Baptist Mission Hospital in Shaohsing, Chekiang Province, through the kindness of Dr. F. W. Goddard and Dr. C. H. Barlow. There were in all 188 specimens carefully preserved in moist alcohol packs. These preserved specimens were grayish-white in color but many of them retained a shade of the original reddish-brown. They measured in length from 17 to 48 mm., in width from 7 to 17 mm., and in thickness from 1 to 4 mm. In some the vitellaria could be clearly outlined through the overlying tissues. In certain specimens the acetabulum was more conspicuous than in others. Some were tongue-shaped, elongated, thin, and flexible; others were oval in shape, firm and stocky. The form varied greatly and it was evident either that *F. buski* was susceptible to marked deviations from a common type or that there were included in this assortment more than one species.

Of the specimens in hand, 18 were stained, cleared and mounted in balsam under very gentle pressure. The cuticle was removed from six. The cirrus pouch was dissected out, stained and mounted from four specimens. Freehand sections

were made from six and microtome sections from five specimens. Ova were removed from the lower metraterm of 12. About half of the total number were photographed. From gross appearances the specimens were divided into two general groups. In Group I were placed the long, flexible flukes with irregular contours and conspicuous vitellaria. Group II included the specimens more nearly elliptical, smoother, thicker and with more prominent ventral suckers. After this arbitrary division had been made, it was found that the flukes in Group II possessed cuticular spines, whereas those in Group I were uniformly unspined. Of the total number, 105 were spined, 83 were smooth.

GROUP I.

The general appearance is that of long, flat, tongue-shaped fasciolopsinæ with irregular contours. The color of specimens after preservation in alcohol is grayish-white with marginal pigmentation representing the distribution of the vitellaria (Fig. 1). In length they measure from 21 to 48 mm., in breadth from 7 to 15 mm. and in thickness from 1.5 to 3.3 mm. The average size of twenty typical mature specimens is 36.7 by 11.2 by 2.1 mm. The surface is smooth and glistening. The dorsum is covered by a much thickened cuticle. There are no cuticular spines.

The ventral sucker is large and muscular, irregularly bell-shaped, with the acetabular disc at its base pointing forward and downward. It is provided with radial and circular muscle fibres. The size and shape of the acetabulum and of its suckorial disc vary in different specimens, depending largely on the contraction or relaxation of its musculature. The ventral sucker measures from 2.65 to 3.0 mm. in length, and from 1.95 to 2.6 mm. in width, with an average of 2.86 by 2.24 mm. The acetabular disc measures from 1.15 to 1.6 mm. in its transverse diameter, and from 0.7 to 1.2 mm. between the anterior and posterior margins.

The cephalic cone is blunt and not clearly defined. The oral sucker projects ventrad from the anterior extremity of

the cephalic cone. Including its musculature it measures from 0.5 by 0.3 mm. to 0.6 by 0.35 mm. The transverse diameter of the oral aperture is from 0.2 to 0.4 with an average of 0.31 mm. The oral canal passes upward and backward through the sucker into a pre-pharyngeal dilatation limited by a pre-pharyngeal sphincter, then through a large globular pharynx, somewhat flattened in its antero-posterior diameter, through a very short esophageal constriction and into the transverse portion of the intestine lying between the pharynx and the cirrus. The pharynx measures from 0.6 to 0.9 mm. by 0.5 to 0.65 mm., averaging 0.7 by 0.58 mm. The cæca pass toward the lateral margins, curve around the ventral sucker and extend backward, the blind ends almost meeting at the posterior extremity. At the level of the shell-gland and between the two testes the cæca curve inward toward the median line. The cæca in this group are characterized by the absence of irregular convolutions, by uniformity in size and by a relatively large lumen. The cæca measure in diameter from 0.25 to 0.45 with an average of 0.36 mm. (Figs. 3, 4, 5).

The male reproductive system consists of large, ramified testes situated in the median field, one behind the other, occupying the posterior two-thirds of the fluke. A delicate vas efferens leading forward from the transverse axis of each testis, passes above and to the side of the shell-gland, over the uterine coils and, joining the vas efferens from the opposite side, enters the cirrus pouch at its posterior extremity. This pouch extends as a large, convoluted muscular tube from a point about midway between the acetabulum and the shell-gland, often nearer the latter, to the ventral sucker where it becomes cylindrical, rapidly narrows, curves over the body of the sucker and terminates in the genital cloaca just in front of the anterior margin of the acetabulum. The convoluted portion is from 3.0 to 5.0 mm. in length, and from 0.55 to 1.3 mm. in diameter. The structure of the cirrus corresponds to that of Group II under which it is more minutely described. The lower portion of the cirrus is evaginated and protruded in 29 out of 55 specimens. The protrusion of the cirrus is accompanied by an evagination of the genital cloaca. This condition closes the opening from the metraterm and perhaps gives predominance, temporarily, to the male functions in the sexual life of this hermaphrodite (Figs. 17, 18, 20).

The vitellaria extend marginally from the level of the acetabulum to the posterior extremity where they intermingle with those from the opposite side. The vitelline acini are exceedingly numerous and vary in size from 0.05 to 0.12 mm. The ducts from these glands unite to form the right and left vitelline ducts which meet and enter the shell-gland located in the anterior portion of the middle third of the fluke. The shell-gland is oval and measures on the average 1.6 by 1.3 mm. Viewed from the dorsal surface a coarsely branched ovary lies to the right and slightly anterior to the shell-gland (Figs. 4, 15). The uterus is much coiled and varies greatly in diameter. Distended portions measure from 0.4 to 0.8 mm. The metraterm extends from the large uterine coils to the cloaca, passing over the acetabulum, parallel with, and to the left of, the ejaculatory duct and opening at the side of the latter in the genital pore.

An excretory vesicle can be demonstrated in mounted specimens. It begins in two main branches, one on each side of, and anterior to, the shell-gland (Fig. 4). These pass backward and join behind the shell-gland from which point the vesicle extends posteriorly, as a median canal with numerous tributary branches, to the foramen caudale. This is a small depression on the dorsal surface, 0.5 mm. from the posterior extremity, surrounded by circular striations giving it a sphincter-like appearance. The caudal extremity frequently shows a small median fissure leading toward the excretory pore (Figs. 4, 16).

The ova are large, oval, thin-shelled, pale yellow in color and contain a nucleus and yolk cells. The operculum is fairly large in eggs taken from the lower portion of the metraterm (Figs. 25, 26, 27). The measurements of 36 typical eggs are:

Length0.120 to 0.138 mm.	Average 0.128 mm.
Width0.072 to 0.094 mm.	" 0.084 mm.
Operculum0.027 to 0.035 mm.	" 0.031 mm.

GROUP II.

The flukes in this group are thick, firm, oval in shape, smaller and more constant in size and form than those of Group I (Fig. 2). The cephalic cone is small but clearly defined on lateral inspection. The specimens tend to assume a dorso-concave position with the cone sharply ventro-flexed. Occasionally this position is reversed. The color of the preserved specimens is lighter than in Group I. The vitellaria cannot be clearly distinguished through the overlying tissues. The measurements of 25 typical specimens are:

Length17.0 to 30.0 mm.	Average 25.4 mm.
Width 7.5 to 13.0 mm.	" 11.4 mm.
Thickness 2.3 to 3.3 mm.	" 2.6 mm.

The surface is smooth and unwrinkled. The dorsal integument is thickened as in Group I but on the ventral surface cuticular spines are present. In some specimens the entire ventral surface is thickly covered; in others the spines are found chiefly on the anterior third and are most numerous in the region about the oral and ventral suckers and along the lateral portion of the ventral surface extending inward about half-way to the median line. In one area a count showed approximately 250 to the square millimeter. Except for small areas on each side of the cephalic cone and for a short distance over the lateral margins, the spines are confined to the ventral surface. There is considerable variation in the size and shape of these cuticular spines. Marginal spines and those on the cephalic cone appear as sharp spicules from 0.04 to 0.07 mm. in length. On the ventral surface they are wedge-shaped, from 0.03 to 0.05 mm. in length, from 0.02 to 0.035 mm. in width and from 0.01 to 0.015 mm. in thickness at the base gradually diminishing toward a distal edge. From above they appear as scales deeply embedded in the cuticle, the free edge being irregular in contour, somewhat rounded and a little broader than the base (Figs. 9, 10, 11, 13, 14).

The ventral sucker presents no variation from the type described under Group I, except that it is appreciably larger.

It measures through its musculature from 2.75 to 3.20 mm. in length, by 2.10 to 2.70 mm. in width and averages 3.01 by 2.34 mm. The oral sucker is subterminal as in Group I. It measures on the average 0.58 by 0.35 mm., while the oral aperture is 0.32 by 0.13 mm. A pre-pharynx is present. The pharynx measures 0.82 by 0.65 mm.

The cæca present certain characteristic variations from those in Group I. In addition to the two typical inward curves there are frequent irregular convolutions especially prominent in the anterior portion of the worm. There are also numerous constrictions and dilatations. The diameter of the gut is from 0.16 to 0.23 mm. whereas in Group I it measures from 0.25 to 0.45 mm. The cæca are relatively longer than in the first group and may be roughly estimated at twice the body length (Figs. 6, 7, 8).

The size of the cirrus pouch and the branching of the testes vary somewhat in the individuals of each group. The ramifications of the testes are perhaps more numerous and denser in the spined than in the unspined worms. The cirrus pouch is convoluted as in Group I, but is less conspicuous and measures from 0.4 to 0.6 mm. in its greatest diameter (Fig. 19). The cirrus is protruded in only a few specimens of this group. As the vasa efferentia enter the adventitious tissue surrounding the cirrus pouch they unite and open, within the cirrus pouch, into the large convoluted portion of the vas deferens. This extends almost to the ventral sucker and constitutes the vesicula seminalis from the anterior portion of which is giving off a large diverticulum. This appendage is projected backward in irregular convolutions beside the seminal vesicle and within the cirrus sac almost to its posterior limit (Figs. 21, 30). The seminal vesicle and its appendage are lined with cylindrical epithelium. The lumen of the diverticulum, or seminal pouch, is larger than that of the seminal vesicle and contains great numbers of spermatozoa. It apparently functionates as a seminal reservoir (Fig. 22). Above the dome of the ventral sucker the vas diminishes to a diameter of 0.2 mm., its muscular structures become more prominent and the epithelium becomes definitely of the columnar type (Fig. 23). This portion of the vas serves as an ejaculatory duct and extends to a point about 2 mm. from the genital pore, where the duct becomes much constricted and is surrounded by a strong muscular sphincter 0.3 mm. in length. Below this sphincter is the cirrus proper, a muscular structure from 0.6 to 0.9 mm. in length, the distal extremity of which projects into the terminal portion of the canal. The latter is approximately the same length as the cirrus. Its lumen varies in size and is beset with numerous minute triangular spines. When the cirrus protrudes through the genital pore, this pre-cirral canal becomes completely evaginated and the spines which line its lumen appear on the surface of the projecting cirrus (Fig. 31).

The vitelline glands are as in Group I, but not usually so closely confined to the lateral margins. The acini vary in size but on the whole are slightly larger than in the unspined worms and measure from 0.07 to 0.16 mm. The shell-gland is noticeably longer in its longitudinal axis. It is oval and measures

from 1.6 to 2.2 mm. by 1.0 to 1.3 mm., with an average of 1.9 by 1.1 mm. The uterus is more tightly coiled than in the first group. Its lumen is smaller and in none of the spined group does it exceed 0.45 mm. in diameter. The location and appearance of the ovary, the course of the metraterm and its opening in the genital pore, the excretory vesicle and the caudal foramen, are as described under Group I.

The ova, similar in general appearance, differ in size and shape and in the relative size of the operculum from those of the unspined worms. The measurement of 64 typical eggs gives the following:

Length	0.130 to 0.160 mm.	Average 0.138 mm.
Width	0.070 to 0.095 mm.	" 0.082 mm.
Operculum	0.016 to 0.032 mm.	" 0.023 mm.

Eggs of very unusual size and those showing distortion or shrinkage are not included. In general, ova from the spined group are longer, relatively narrower and possess a more delicate operculum than those of the flukes under Group I (Figs. 28, 29, 30).

With minor exceptions the specimens of Group I correspond to the accepted descriptions of *F. buski*. Mature worms, however, differ from the description given by Odhner in that the cirrus pouch is definitely convoluted, the shell-gland is oval and located in the anterior portion of the middle third of the fluke. *F. fülleborni*, as described, bears a very close resemblance to the flukes of Group I. The location, size and shape of the shell-gland, the large convoluted cirrus sac, the absence of cuticular spines and other general characteristics would seem to identify the largest of our parasites with this species. In Group I, however, there are mature, uncontracted worms much smaller than those described by Rodenwaldt. The gradation in size from smallest to largest is complete and structural characteristics remain constant. Reported measurements of the ventral and oral suckers have led to confusion. Some observers give the dimensions of the acetabular disc, some of the acetabular ring, whereas others include the entire musculature of the organ. This fact may account for the discrepancy in measurements between this and other reports.

The presence of cuticular spines was not mentioned in the earliest descriptions of fasciolopsinae from China. The pressure used in mounting specimens is often sufficient to squeeze the soft, thick dorsal cuticle over the edge of the parasite and thus obscure marginal spines. Ventral spines are not easy to demonstrate with the methods ordinarily employed.* Specimens from Cochin-China, presented to the Hygienic Laboratory of the United States Public Health Service, by Barrois and Noc and designated by them as *F. buski*, were found on examination to possess cuticular spines. Leiper (1911) reports the presence of spines in both *F. rathouisi* and *F. goddardi*. Heanley (1908) states that all *F. buski* in South

* To determine the presence of spines, immerse the fluke, ventral surface upward, in water and with a strong light directed from above (a small arc is desirable) examine under the microscope using a No. 3 objective and a high ocular. Transmitted light will reveal marginal spines. Portions of the cuticle may be removed and mounted for examination under higher magnification.

China are spined. Commenting upon this observation Leiper suggests that spines may be characteristic of all fasciolopsinæ and that the decidual character of the integument explains the absence of spines in specimens described as *F. buski*. It is possible that vigorous manipulation or the action of chemicals used in the preservation of specimens or the preparation of mounts may result in disintegration of the cuticular layer, and yet in our experience the material studied has been subjected to all customary laboratory methods including embedding and sectioning without evidence of extensive desquamation and without destroying the spinous character of the integument.

It may be contended that the possession of spines represents only a stage in the life history of these parasites. This is improbable, as both young and fullgrown specimens are found in each group and there are, moreover, other less conspicuous features already enumerated, characteristic of each group, which remain constant notwithstanding wide variations in size and development. Since both auto-copulation and cross-copulation occur among trematodes it is not inconceivable that in such closely allied species hybrid forms might appear. Such an assumption would not militate against the consideration of these two groups as distinct species, conveniently differentiated by the presence or absence of cuticular spines.

Except for the presence of spines, the smaller parasites in Group II correspond closely to Ward's description of *F. rathouisi* but not to Poirier's original account upon which the species was founded. It is recognized that Poirier's report was incomplete and based upon a single poorly mounted specimen which so careful an investigator as Odhner has identified as a contracted form of *F. buski*. *F. rathouisi* as described by Ward is, according to his own account, very similar to his *F. goddardi*. Jeffries and others do not consider the distinction substantiated. Through the kindness of Dr. Ward it has been possible to examine a cleared and mounted co-type specimen of *F. goddardi*. This specimen was secured from the same locality as the flukes we have described. It measures 24 by 11.5 mm. The ventral sucker is 3.2 mm. in length, by 2.5 in width. The acetabular disc measures 1.6 by 1.0 mm. The oral sucker is 0.6 by 0.47 mm., with an aperture 0.3 by 0.18 mm. The cirrus is not conspicuous. The cæca are irregularly curved, show constrictions and dilatations and measure from 0.16 to 0.20 mm. in diameter. The surface shows evidences of disintegration and no cuticular spines could be demonstrated. In structure *F. goddardi* resembles the parasites of Group II. The spined flukes which we have described occasionally present slight variations in the branching of the testes, in the size of the vitelline acini and in the distention of the uterine coils. These variations are inconstant and may be due to different phases of functional activity. In general the specimens exhibit such morphological uniformity that a further subdivision does not, at this time, seem justifiable.

That there are, however, spined and non-spined fasciolopsinæ in China is indicated by Jeffries who in 1911 stated that "the South China variety has cuticular spines on the anterior part of the body and is a more fleshy fluke than the speci-

mens from Mid-China, in which, too, the spines are absent." The existence of a spined and a non-spined species is also suggested by the conflicting reports as to the presence of spines on *F. buski*, depending largely upon the locality from which the specimens have been secured, and by the finding of spines on alleged species closely allied to *F. buski*. That Group II is not *F. buski* is evident from the statement in the original description, and in subsequent reports by Looss, Stiles, and Odhner, that the cuticle of *F. buski* is smooth, and by other less conspicuous variations in form and structure. *F. fülleborni* is described as a non-spined fluke differing in this and other respects from the spined group. That it is not *F. rathouisi* is evident from the specific statement by Poirier that the fluke described by him does not possess cuticular spines and by the absence of any reference to such structures in the later description by Ward. Odhner has moreover re-examined the type specimen and believes it identical with *F. buski*. That the spined species may be *F. goddardi* is suggested by the close morphological resemblance and by Leiper's statement that *F. goddardi* is spined. Against this view is the original report by Ward in which cuticular spines are not mentioned and our failure to demonstrate these structures upon re-examination of a co-type specimen. Under these conditions it is difficult to identify Group II with any described species and inasmuch as the spinous character is so distinctive a feature of this group, it is presented as a separate species appropriately designated *Fasciolopsis spinifera*, in which may be included the flukes described as *F. buski*, or one of the allied species, which differ from the standard type in the possession of cuticular spines. Should further examination of the original type specimens satisfactorily establish their identity with Group II, the older designation may be employed and the proposed term be regarded only as a descriptive synonym.

In reporting this investigation the purpose is not to complicate further the classification by adding another species, but rather to present these two groups of parasites from the Orient in the hope that this and future studies may lead to a more satisfactory classification and to a better knowledge of the fasciolopsinæ. It is a pleasure to express my appreciation of the many courtesies received from the staff of the Johns Hopkins Hospital and to acknowledge my indebtedness to Dr. Charles W. Stiles of the United States Public Health Service, for his painstaking examination of the material upon which this report is based and for his valuable assistance in questions of classification and nomenclature.

CONCLUSIONS.

The species *Fasciolopsis buski* is subject to variations in size and form and in the relative prominence of internal structures depending on its maturity, its environment and perhaps upon the phase of sexual activity.

Closely related to *Fasciolopsis buski* is a distinct species represented here by Group II, the chief characteristic of which is the possession of cuticular spines. For this species the name *Fasciolopsis spinifera* is proposed.

TABULATED SYNOPSIS

Fasciolopsis buski. *Fasciolopsis fülleborni*. *Fasciolopsis rathouisi*.

Name.	Described by.	Size.	Shape.	Cuticular spines.	Ventral sucker.	Oral sucker.	Pharynx.
<i>D. buski</i> . <i>D. crassum</i> . <i>F. buski</i> .	Lankester, 1857. Cobbold, 1859. Looss, 1899. Stiles, 1901. Odhner, 1902.	Length, 24-45 mm. Width, 6-12 mm. Thickness, 1.5-4 mm. Also, Length, 24-70 mm. Width, 5.5-14 mm.	Elongated, nearly oval. Indefinite cephalic cone.	Absent.	Diameter 1.6 to 2 mm.	Subterminal. Diam. 0.5 mm.	Globular. Diam. 0.7 mm.
<i>F. fülleborni</i> .	Rodenwaldt, 1909.	Length, 30-50 mm. Width, 14-16 mm. Usually, 50 by 14 mm.	Tongue-shaped. Cephalic cone not clearly defined.	Absent.	2.6 by 2.9 mm.	Circular. Subterminal. Diam. 0.75 mm.	Diam. 0.7 mm.
F. of Group I. (<i>F. buski</i> .)		Length, 21-48 mm. Width, 7-15 mm. Thickness, 1.5-3.3 mm. Average of mature worms: Length, 36.7 mm. Width, 11.2 mm. Thickness, 2.1 mm.	Elongated, irregularly oval, tongue-shaped. Short, blunt cephalic cone not well defined.	Absent.	Length, 2.65-3.0 mm. Width, 1.95-2.6 mm. Average, 2.86 x 2.24 mm. Acetabular Disc. 1.15 to 1.6 by 0.7 to 1.2 mm. Average, 1.4 x 0.95 mm.	Subterminal, 0.5 x 0.3 to 0.6 x 0.35 mm. Oral aperture, Diam. 0.2-0.4 mm. Aver. 0.31 mm.	Globular, somewhat flattened. 0.6 to 0.9 by 0.5 to 0.65 mm. Average, 0.7 x 0.57 mm.
<i>D. rathouisi</i> . <i>F. rathouisi</i> .	Poirier, 1887. Ward, 1903.	Length, 15-19 mm. Width, 8.5-10.5 mm. Thickness, 3 mm. (Ward.) 25 x 16 mm. (Piorier)	Bluntly oval or elliptical with short cephalic cone.	Absent. (Poirier, Ward.) Present. (Leiper.)	1.32 to 1.38 by 0.68 to 0.7 mm.	Subterminal, 0.25 to 0.29 by 0.2 mm.	
<i>F. goddardi</i> .	Ward, 1909.	Length, 21-22 mm. Width, 9 mm.	Oval. Longer and more slender than <i>F. rathouisi</i> .	Absent. (Ward.) Present. (Leiper.)		Smaller than in <i>F. buski</i> or <i>F. rathouisi</i> .	
F. of Group II. (<i>F. spinifera</i> .)		Length, 17-30 mm. Width, 7.5-13 mm. Thickness, 2.3-3.5 mm. Average of mature worms: Length, 25.4 mm. Width, 11.4 mm. Thickness, 2.6 mm.	Oval. Stocky. More fleshy than <i>F. buski</i> . Cephalic cone small but well defined on lateral inspection.	Present on ventral surface and margins. Most numerous on anterior third.	Length, 2.75-3.2 mm. Width, 2.1-2.7 mm. Average, 3.01 x 2.34 mm. Acetabular Disc. 1.45 to 1.70 by 0.70 to 1.05 mm. Average, 1.60 x 0.88 mm.	Subterminal. Average size, 0.58 x 0.35 mm. Oral aperture, Diam. 0.32 mm.	Globular, flattened. 0.82 x 0.65 mm. Lumen, 0.22 mm

OF CHARACTERISTICS.

Fasciolopsis goddardi. Group I, *F. buski*. Group II, *F. spinifera*.

Cæca.	Cirrus pouch.	Vitellaria.	Shell-gland.	Testes.	Uterus.	Excretory vesicle.	Ova.
Lateral, unbranched, with two characteristic curves toward the median line.	Conspicuous, straight, cylindrical sac, .25 to .33 mm. in diameter. Extends half way to shell-gland. Contains seminal vesicle and peculiar cæcal appendage.	Marginal. Acini small and numerous.	Round. Diameter, 1.0 to 1.5 mm. Located about middle of body.	Dendritic. Posterior to shell-gland, one behind the other in median line.	Large open coils. Anterior to shell-gland.	Tubular. Excretory pore at posterior extremity.	Thin-shelled. Operculated. 120 to .130 by .077 to .080 mm.
As in <i>F. buski</i> .	Prominent, convoluted sac, diameter, 1 mm. Extends two-thirds of distance to shell-gland. Contains convoluted, saccular seminal vesicle. No cæcal appendage observed.	Similar to <i>F. buski</i> in distribution. Acini strikingly small.	Almond-shaped. 2.3 x 1.2 mm.	Regularly branched. Separated by incurving cæca. Anterior smaller than posterior.	As in <i>F. buski</i> . Large distended coils.	Median stem with transverse branches. Caudal foramen.	Thin-shelled. Operculated. Length, .100 Width, .073
Lateral, unbranched, with two regular curves as in <i>F. buski</i> . Diameter uniform, measures from 0.25 to 0.45 mm. Average diameter, 0.36 mm.	Conspicuous, convoluted sac. Extends half to two-thirds distance to shell-gland. Contains seminal vesicle and large diverticulum. Cirrus frequently protrudes. Convoluted portion is from 0.55 to 1.30 mm. in diameter.	Marginal. Acini small and numerous; vary in diameter from 0.05 to 0.12 mm.	Oval. Located in anterior part of middle third. Measures, 1.35 to 1.80 by 1.00 to 1.45 mm. Average, 1.6 x 1.3 mm.	Extensive ramifications. Conspicuous transverse axes. Irregular sacculations in old worms.	Large coils, densely packed with ova. Maximum diameter 0.4 to 0.8 mm.	Median canal dividing near shell-gland. Numerous tributary branches. Caudal foramen on dorsal surface near posterior extremity.	Thin-shelled. Operculated. Length, .120-.138 mm. Width, .072-.094 mm. Operc., .027-.035 mm. Average, Length, .128 mm. Width, .084 mm. Operculum, .031 mm.
More irregular than in <i>F. buski</i> and with more pronounced curves.	Convoluted. Not so conspicuous as in <i>F. buski</i> .	Distribution slightly different from <i>F. buski</i> . Acini more numerous.		More compactly branched, broader and denser than in <i>F. buski</i> .	Broad, heavy, closely grouped coils.		Oval, thin-shelled, with delicate operculum. Length, .150 mm. Width, .080 mm.
		Acini larger and more conspicuous than in <i>F. buski</i> .			Very closely coiled.		
Curves pronounced and frequent. Irregularly looped. Numerous constrictions and dilatations. Diameter small, 0.16 to 0.23 mm. Average, 0.20 mm.	Convoluted sac as in Group I, but smaller and not so prominent. Diverticulum present. Cirrus seldom protrudes. Convoluted portion is from 0.4 to 0.6 mm. in diameter.	Acini slightly larger than in Group I, measuring in diameter from 0.07 to 0.16 mm.	Oval. Longer and narrower than in Group I. Measures, 1.6 to 2.2 by 1.0 to 1.3 mm. Average, 1.9 x 1.1 mm.	Ramifications more numerous and denser than in Group I.	More tightly coiled than in Group I. Lumen smaller. Diameter does not exceed 0.45 mm.	Median canal with tributary branches. Caudal foramen on dorsal surface near posterior extremity.	Thin-shelled with small, delicate operculum. Length, .130-.160 mm. Width, .070-.095 mm. Operc., .016-.032 mm. Average, Length, .138 mm. Width, .082 mm. Operculum, .023 mm.

It may be desirable to simplify the present classification and group the species of *Fasciolopsis* heretofore described into these two species distinguished by the presence or absence of cuticular spines.

REFERENCES.

- Fasciolopsis buski*, *rathouisi*, *goddardi* and *fülleborni*.
Barrois, Th., et Noc, F. (1908): Sur la fréquence du *F. buski* en Cochinchine. Bull. Soc. pathol. exot., Paris, I, pp. 216-221.
Brau, P. (1912): Parasitisme intestinal du porc de Cochinchine. Bull. Soc. méd.-chir. de l'Indo-Chine, Hanoi et Haifong, III, pp. 585-587.
Castellani and Chalmers (1913): Man. of Trop. Med., pp. 472, 473.
Cobbold, T. S. (1860): Synopsis of the Distomidae. Jour. Proc. Linnean Soc., London, I, p. 1.
Idem (1875): On the Supposed Rarity of *Distomum crassum*. Jour. Proc. Linnean Soc., London, XII, p. 285.
Idem (1879): Parasites: A Treatise on the Entozoa of Man and Animals. London.
Goddard, F. W. (1907): Two Rare Fasciolidae. China Medical Journal, XXI, pp. 195-198.
Heanley, C. M. (1908): A Large Fluke of Man Probably not Hitherto Described. *F. buski* as a Parasite of Man in Hongkong; its usual host probably the pig. Jour. Trop. Med. & Hyg., XI, pp. 122, 123.
Jeffries, W. H. (1910): Diseases of China, Jeffries and Maxwell, pp. 183-188.
Lankester, E. R. (1857): Manual of Animal and Vegetable Parasites, Appendix B, p. 437.
Leiper, R. T. (1911): On Kwan's Fluke and the Presence of Spines in *Fasciolopsis*. Jour. Trop. Med. & Hyg., XIV, pp. 119, 120.
Looss, A. (1899): Weitere Beiträge zur Kenntnis der Trematoden-Fauna Aegyptens, zugleich Versuch einer maturalichen Gliederung des Genus *Distomum retzius*. Zool. Jahrb. Syst., XII, pp. 521-784.
Idem (1907): Some Parasites in the Museum of the School of Tropical Medicine, Liverpool. An. Trop. Med. & Par., I, pp. 123-152.
Idem (1914): Handbuch der Tropenkrankheiten, Carl Mense. Vol. II, pp. 375, 376.
Lyngdoh, H. (1906): *Distomum crassum*, Indian Med. Gaz., Calcutta, XLI, pp. 405, 406.
Mathis, C., et Leger, M. (1911): *F. buski* au Tonkin, Son extrême rareté chez l'homme; sa fréquence chez le porc. Bull. Soc. pathol. exot., Paris, IV, pp. 200-202.
Idem (1911): Recherches de Parasitologie et de Pathologie, humaine et animale, au Tonkin., pp. 188-190.
Maxwell, J. L. (1911): Research Report. China Med. Jour., Shanghai, Jan., pp. 166-173.
Moore, J. T., and Terrill, J. J. (1905): *Fasciolopsis buski*; the first case reported in the United States; found in a patient dying of typhoid fever. Jour. Am. Med. Assn., XLV, pp. 1002-1003.
Nicol, B. (1910): *Fasciolopsis buski* in Natal. Jour. Trop. Med. and Hyg., XIII (Nov. 15), p. 341.
Odhner, Th. (1902): *Fasciolopsis buski*, ein bisher wenig bekannter Parasit des Menschen in Ostasien. Cent. Bakt. u. Par. Jena, XXXI, pp. 573-581.
Idem (1908): Was ist *Distomum rathouisi*? Arch. Parasitol. XII, pp. 467-471.
Poirier, P. (1887): Note sur une nouvelle espèce de Distome, parasite de l'homme, le *Distomum rathouisi*. Arch. zool. exp. génér. (2), V, p. 203.
Rodenwaldt, E. (1909): *Fasciolopsis fülleborni*. Centrbl. Bakt., Parasit. u. Infect., Jena, L, pp. 451-461.
Idem (1909): Ein neuer Trematode, *Fasciolopsis fülleborni*. Verh. Deutsch. tropen-med. Ges., Arch. Schiffs. u. Trepenhyg., XIII, p. 305.
Stephens, J. W. W. (1916): Animal Parasites of Man (after Braun). Fathan, Stephens, and Theobald, pp. 245-249.
Stiles, C. W. (1901): Illustrated Key to the Trematode Parasites of Man.
Ward, H. B. (1903): Trematoda. Wood's Ref. Handb. Med. Sciences, VII, pp. 859-874.
Idem (1908): Data for the Determination of Human Entozoa, II. (Studies from the Zool. Lab., Univ. of Nebraska, No. 86.) Trans. Amer. Micr. Soc., XXVIII, pp. 177-202.
Idem (1909): *F. buski*, *F. rathouisi* and Related Species in China. (Studies from the Zool. Lab., Univ. of Nebraska, No. 94.) China Medical Journal, XXIV (Jan., 1910), pp. 1-10.

DESCRIPTION OF FIGURES.

FIG. 1.—*F. buski*. Unspined fasciolopsinæ from Group I. Actual size. Ventral surface.

FIG. 2.—*F. spinifera*. Spined fasciolopsinæ from Group II. Actual size. Ventral surface.

FIGS. 3, 4 and 5.—*F. buski*. Unspined fasciolopsinæ from Group I, stained, cleared and photographed with transmitted light. Twice actual size. No. 3 is the dorsal view of a small specimen. The shell-gland is centrally located and almost spherical. Nos. 4 and 5 represent mature flukes of this group, showing the oval shell-gland, the cæca with typical curves, the convoluted cirrus pouch and the protruding cirrus. No. 4 is a dorsal view and shows the caudal foramen and the excretory canal bifurcating near the shell-gland. Portions of the excretory sinus have retained the hæmatoxylin stain. In No. 5 the ventral surface is uppermost. In all three specimens the vitellaria intermingle near the posterior extremity.

FIGS. 6, 7 and 8.—*F. spinifera*. Spined fasciolopsinæ from Group II. Twice actual size. Figs. 6 and 7 are stained and mounted with the ventral surface uppermost. They show irregularly convoluted cæca of relatively small diameter. The shell-gland is oval. Ramifications of the testes are denser and coarser than in Figs. 3, 4 and 5. Fig. 8 is from an unstained specimen and shows the excretory system consisting of a median canal with numerous tributary branches.

FIG. 9.—*F. spinifera*. Marginal spines from a mounted specimen of Group II. (From specimen shown in Fig. 7.) $\times 125$.

FIG. 10.—*F. spinifera*. Cuticular spines on ventral surface at level of acetabulum. From sagittal section of specimen from Group II. Hæm. & Eosin. $\times 250$.

FIG. 11.—*F. spinifera*. Cuticular spines on ventral surface between acetabulum and shell-gland. Transverse section of specimen from Group II. Hæm. & Eosin. $\times 250$.

FIG. 12.—*F. spinifera*. Dorsal cuticle. Transverse section of specimen from Group II. Hæm. & Eosin. $\times 250$.

FIG. 13.—*F. spinifera*. Cuticular spines on ventral surface of fluke from Group II. Masses of vitelline acini are seen through the cuticle. Unstained. $\times 30$.

FIG. 14.—*F. spinifera*. Ventral surface of fluke from Group II showing scale-like character of cuticular spine. Unstained. $\times 125$.

FIG. 15.—*F. buski*. Oval shell-gland and branched ovary from an unspined fluke of Group I. (Fig. 5.) Uterine coils are seen above and ramifications of the testes below. $\times 15$.

FIG. 16.—*F. buski*. Foramen caudale, showing annular striations and caudal fissure. $\times 75$.

FIG. 17.—*F. buski*. Convoluted cirrus pouch from an unspined fluke (Fig. 4.) Dorsal view. Cirrus is deeply stained. Faintly stained structure parallel with, and to the left of, the cirrus is the metraterm. Cæcum at extreme left. Posterior portion of the pouch is obscured by distended uterine coils. $\times 14$.



FIG. 1.



FIG. 2.



FIG. 3.



FIG. 4.

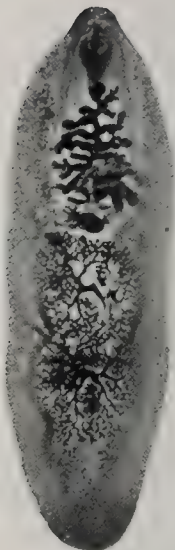


FIG. 5.



FIG. 6.



FIG. 7.

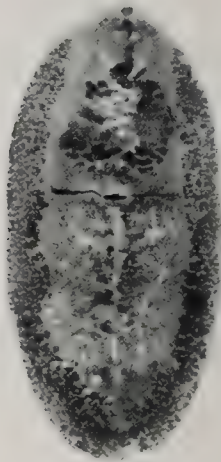


FIG. 8.



FIG. 9.

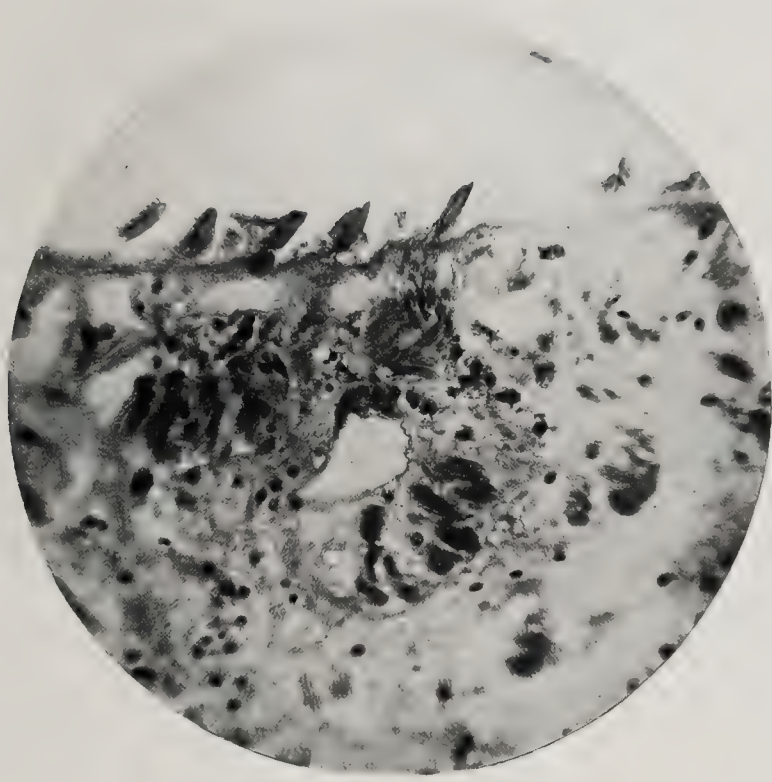


FIG. 10.

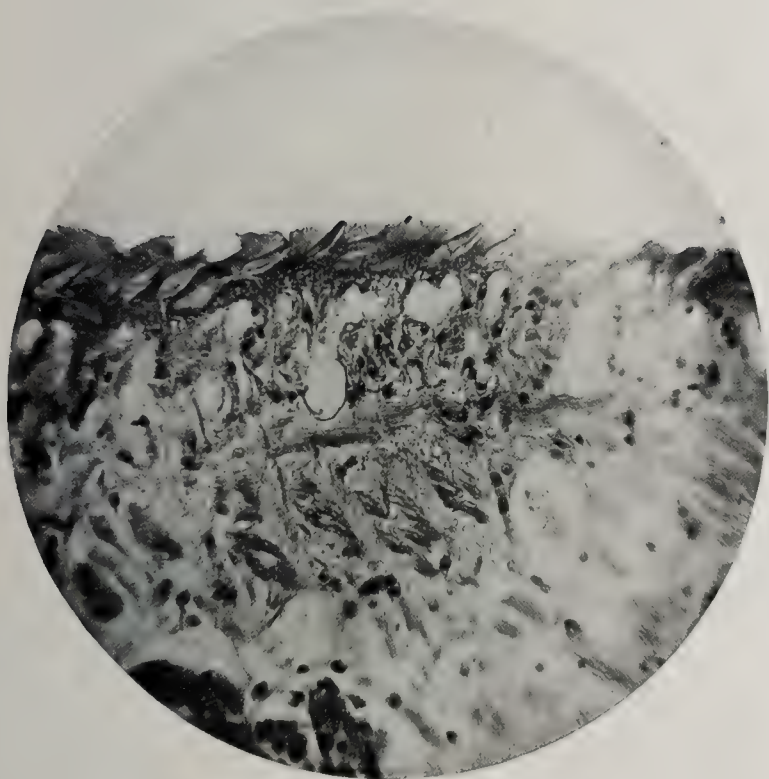


FIG. 11.



FIG. 12.



FIG. 13.

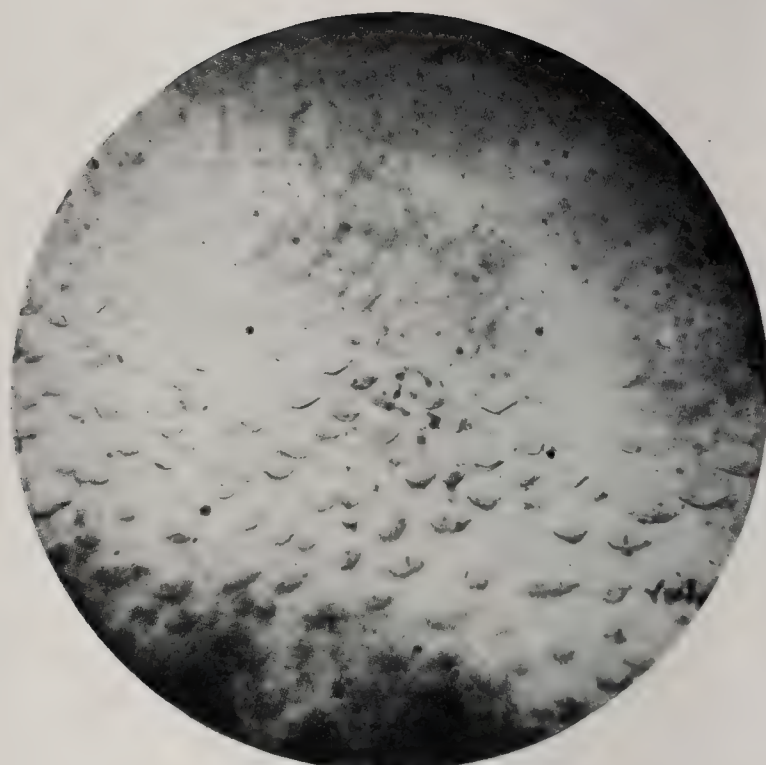


FIG. 14.

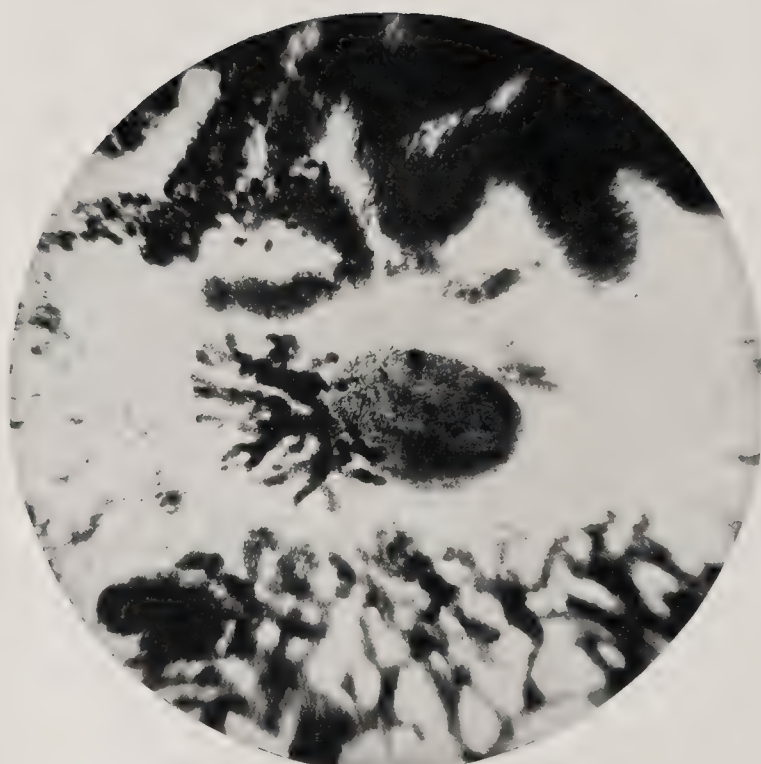


FIG. 15.

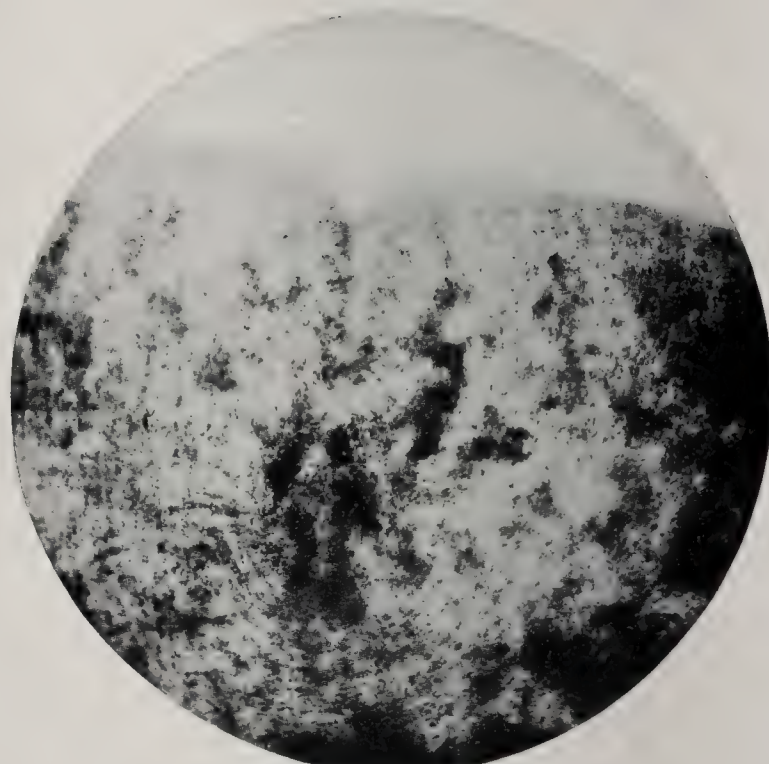


FIG. 16.

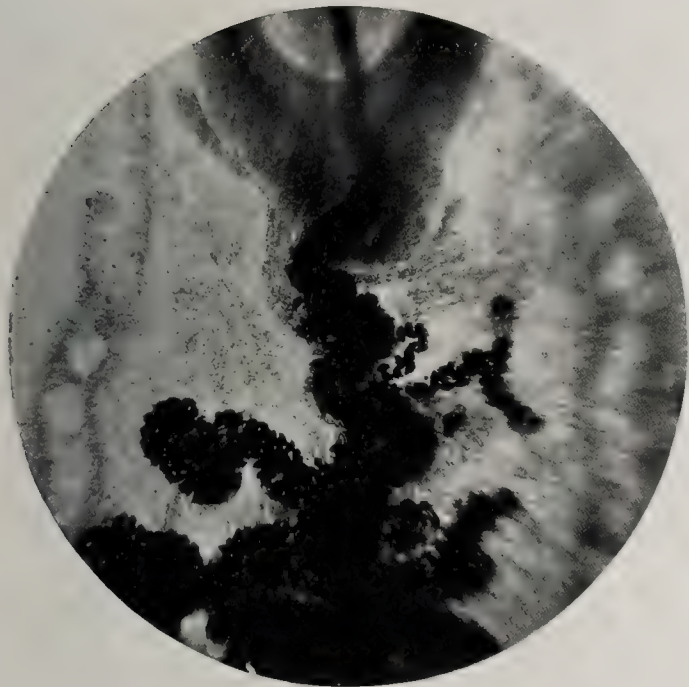


FIG. 17.

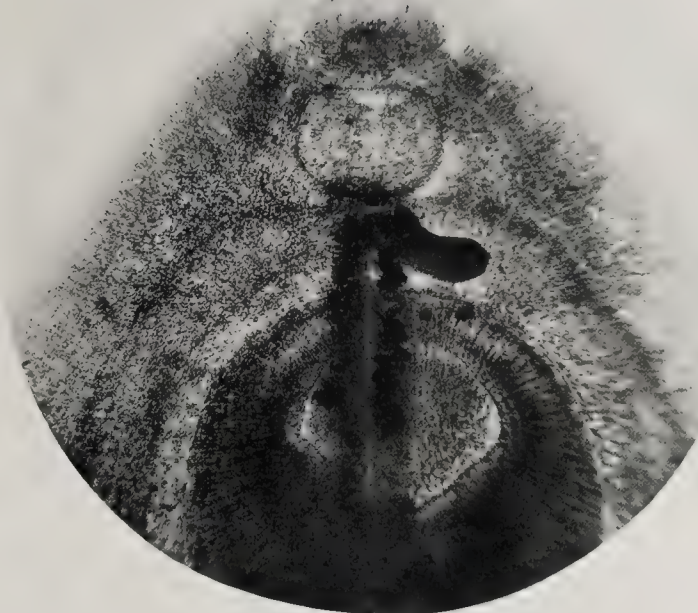


FIG. 18.

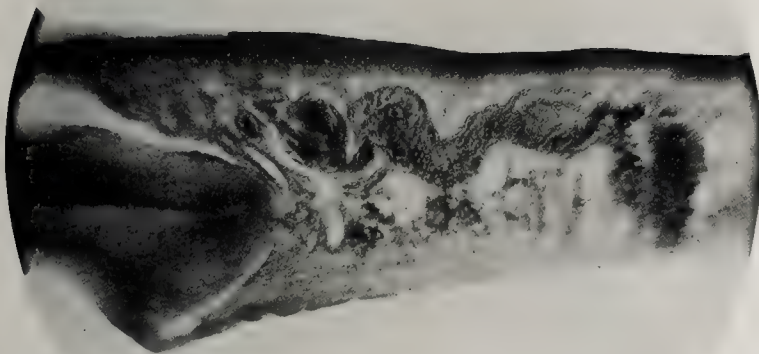


FIG. 19.

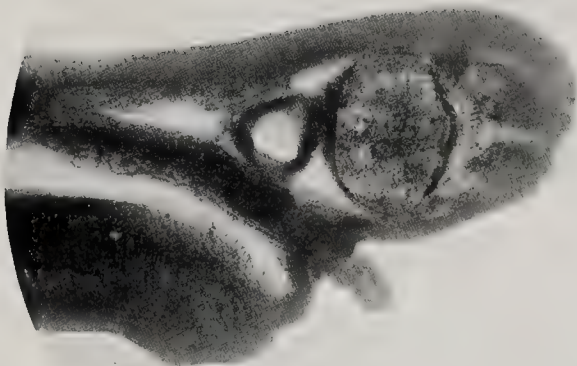


FIG. 20.

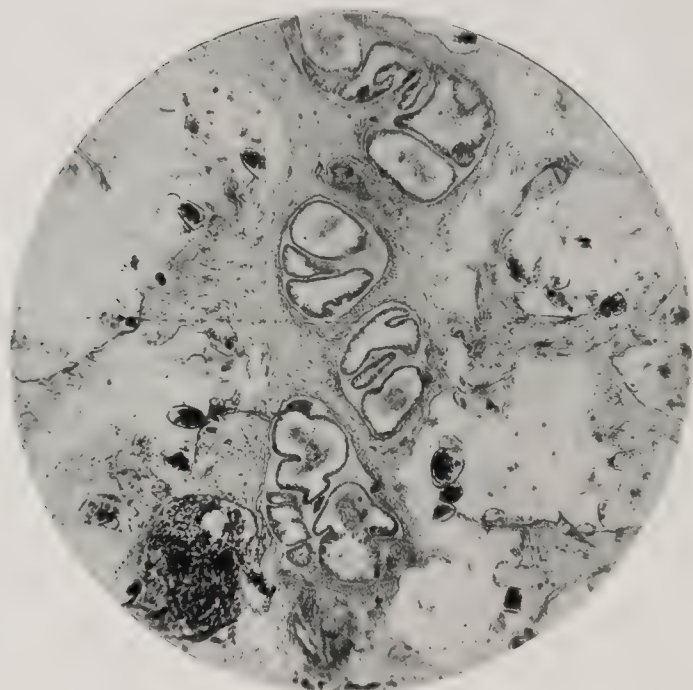


FIG. 21.

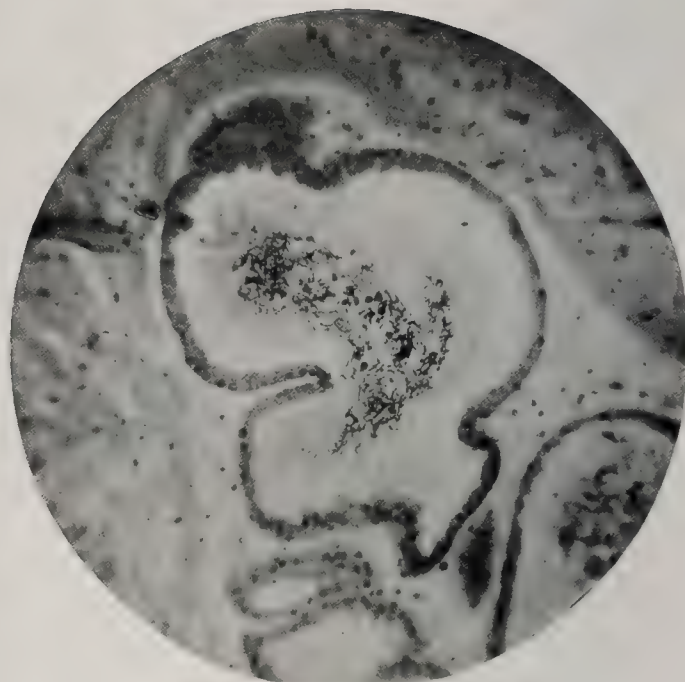


FIG. 22.

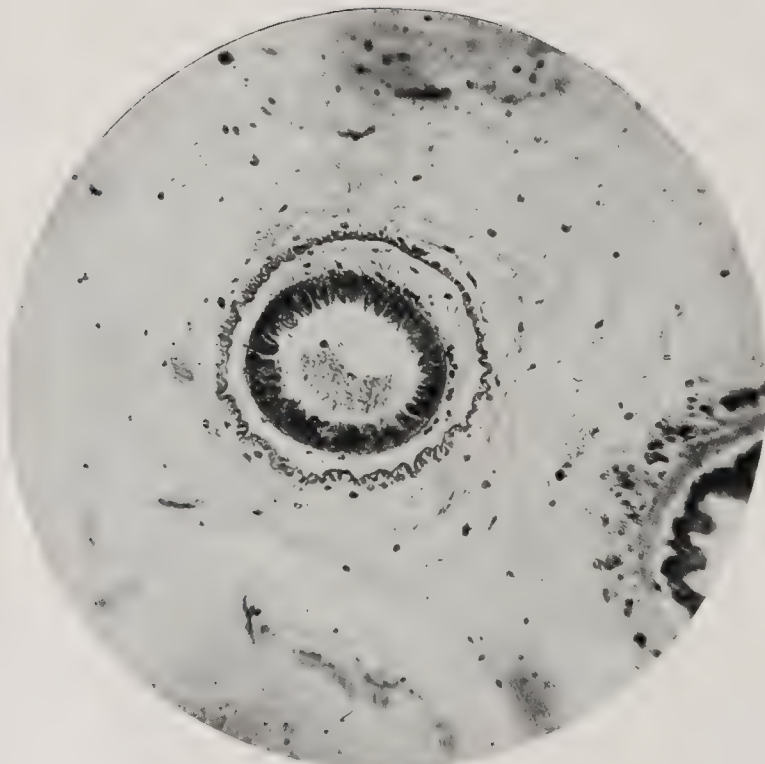


FIG. 23.

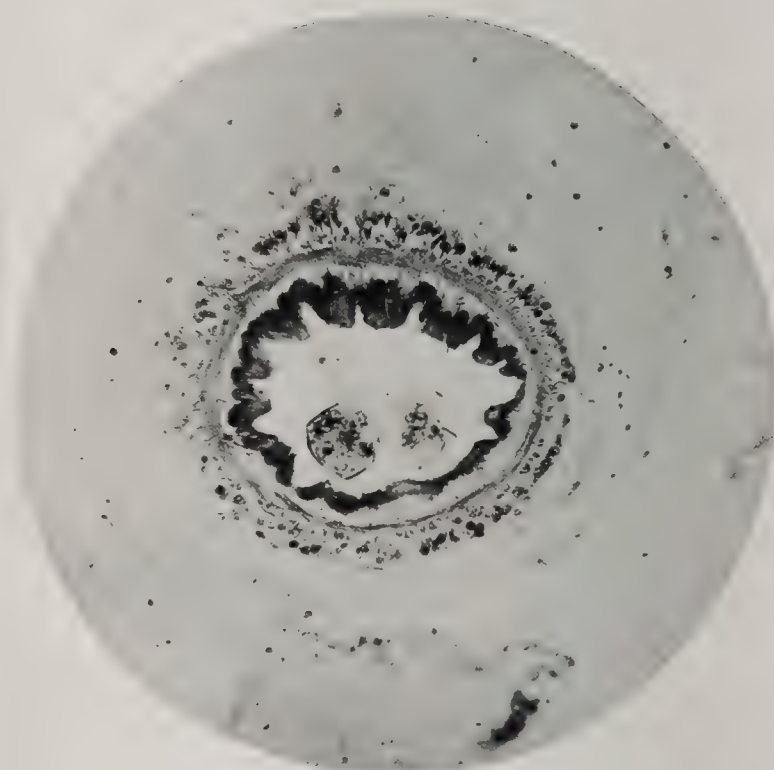


FIG. 24.

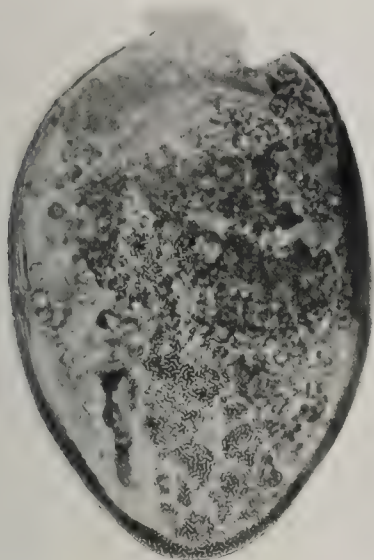


FIG. 25.

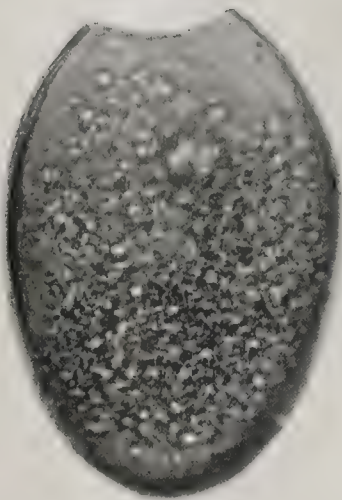


FIG. 26.

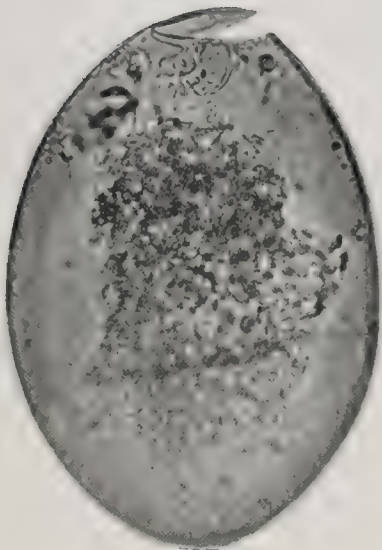


FIG. 27.

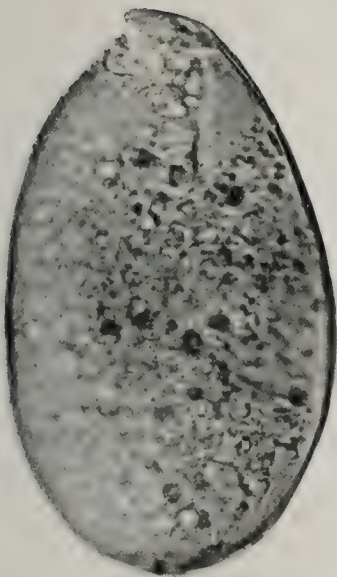


FIG. 28.

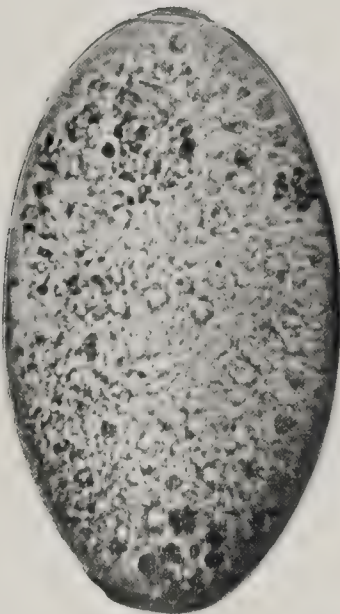


FIG. 29.

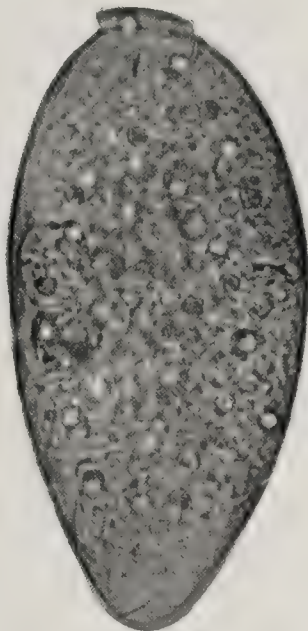


FIG. 30.

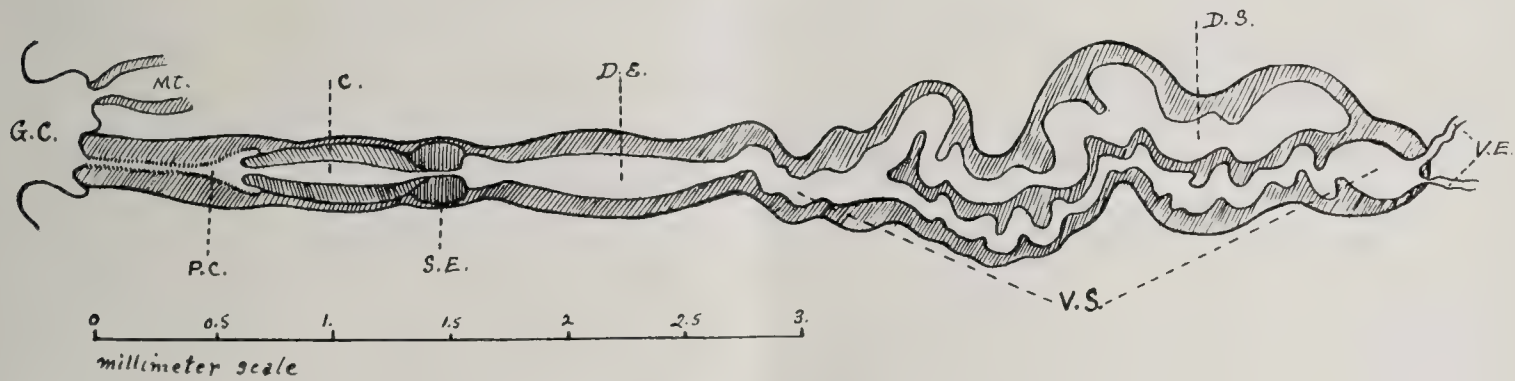


FIG. 31.

FIG. 18.—*F. buski*. Anterior extremity of an unspined fluke (Fig. 5). Ventral view. Structures from above downward are: oral sucker, globular pharynx, cirrus protruding through genital pore and the acetabulum through which can be seen the metraterm and the ejaculatory duct. The cæca appear curving around the acetabulum and meeting just behind the pharynx. $\times 20$.

FIG. 19.—*F. spinifera*. Free-hand sagittal section through anterior portion of a fluke from Group II, showing the convolutions of the cirrus pouch. $\times 14$.

FIG. 20.—*F. buski*. Free-hand sagittal section through the cephalic cone of an unspined fluke. Structures from right to left are: oral sucker, prepharynx, pharynx, transverse section of cæcum, ejaculatory duct and the anterior lip of the ventral sucker. The cirrus projects through a partially everted genital pore. $\times 30$.

FIG. 21.—*F. spinifera*. Horizontal section through the posterior portion of the cirrus pouch showing the convoluted seminal vesicle and its diverticulum in cross-section. Near the lower edge of the section the vasa efferentia may be seen entering the cirrus pouch. Hæm. & Eosin. $\times 30$.

FIG. 22.—*F. spinifera*. Cross-section of the seminal diverticulum from the same section as Fig. 21, but under higher magnification. Within its lumen are large numbers of spermatozoa. Hæm. & Eosin. $\times 160$.

FIG. 23.—*F. spinifera*. Cross-section of the ejaculatory duct at the level of the acetabular disc. Hæm. & Eosin. $\times 160$.

FIG. 24.—*F. spinifera*. Cross-section of the metraterm from same section as Fig. 23. Hæm. & Eosin. $\times 160$.

FIGS. 25, 26 and 27.—*F. buski*. Typical ova from flukes of Group I.

FIG. 25.—Length, 0.118 mm. Width, 0.082 mm. Operculum, 0.030 mm.

FIG. 26.—Length, 0.118 mm. Width, 0.078 mm. Operculum, 0.030 mm.

FIG. 27.—Length, 0.124 mm. Width, 0.086 mm. Operculum, 0.028 mm.

FIGS. 28, 29 and 30.—*F. spinifera*. Typical ova from flukes of Group II.

FIG. 28.—Length, 0.132 mm. Width, 0.076 mm. Operculum, 0.020 mm.

FIG. 29.—Length, 0.140 mm. Width, 0.078 mm. Operculum, 0.018 mm.

FIG. 30.—Length, 0.144 mm. Width, 0.070 mm. Operculum, 0.018 mm.

FIG. 31.—Composite outline of structures within the cirrus pouch. From camera lucida drawings.

V. E. Vasa efferentia.

V. S. Seminal vesicle, 2.5 to 4.0 mm.

D. S. Seminal diverticulum, 2.0 to 3.0 mm.

D. E. Ejaculatory duct, 1.2 to 1.5 mm.

S. E. Ejaculatory sphincter, 0.3 mm.

C. Cirrus proper, 0.6 to 0.9 mm.

P. C. Pre-cirral canal, 0.6 to 1.0 mm.

G. C. Genital cloaca.

Mt. Metraterm.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

MARCH 5, 1917.

1. Exhibition of Case of Cerebro-Spinal Meningitis. DR. V. P. W. SYDENSTRICKER.

C. T., white, aged 21 years, laborer, entered the hospital on January 25, 1917, complaining of sore throat, headache and general malaise. The family history was negative with reference to the present illness. The patient has been blind in his left eye since birth.

His present illness began 24 hours before admission with a slight sore throat and headache. The headache increased rapidly in severity and was accompanied by a marked prostration. Eight hours before admission the patient began to have violent nausea with vomiting, accompanied by some pain at the back of his neck and in all the back muscles.

On admission the temperature was 102.4°, the pulse 188, respirations 30. The patient was semi-delirious, lying in bed with his head retracted, the thighs and legs flexed. He was restless, moaned constantly and complained of pain in the back of the neck. Scattered over the shoulders, thorax, abdomen and legs were numerous bright red petechial spots, varying in size from a pin-head to a dime. There was marked tenderness over the occipital region and neck. The neck was completely rigid. The right pupil was dilated. There was marked photophobia, and a moderate amount of conjunctival injection. The E. O. movements were normal. The conjunctiva of the left eye was markedly injected. There was a subconjunctival hæmorrhage. The left cornea was entirely opaque. The lips were covered with sordes. The mouth was foul, the tongue heavily coated. The tonsils and pharynx were injected. The lungs and heart were negative. The abdomen was negative except for a large, soft spleen. The hands and arms showed a coarse tremor. All the deep reflexes were slightly increased. The Kernig and Brudzinski's signs were positive. W. B. C. 21,000.

A lumbar puncture, on admission, gave a turbid, almost purulent fluid. Twenty cubic centimeters of antimeningococcus serum were injected. Smears from this spinal fluid showed many gram-negative, biscuit-shaped diplococci, both intracellular and extracellular. Cultures gave many colonies of the meningococcus.

Lumbar puncture was repeated at 10.30 a. m. on the next day (January 26). Twenty cubic centimeters of serum were injected. During the day the symptoms increased in severity. The pulse fell to 60 per minute, the respirations to 14 per minute. There was definite choking of the right optic disc.

Lumbar puncture was repeated at 5 p. m. Only 10 c. c. of fluid could be obtained. It seemed clear that there was an obstruction to the descent of the cerebro-spinal fluid probably from massive exudate at the base of the brain.

At midnight Dr. Dandy trephined the cranium in the right fronto-parietal region and punctured the right lateral ventricle. There was an immediate escape of a large amount of turbid fluid under high pressure. The operation was done under primary ether anæsthesia. Immediately after the ventricular puncture the pulse and respirations increased in rapidity.

January 27.—No marked change in patient's symptoms. Lumbar puncture at 10 a. m. and 10 p. m. Forty cubic centimeters of antimeningococcus serum were injected each time. At 5 p. m. 60 c. c. of antimeningococcus serum given intravenously.

January 28.—Lumbar puncture at 10 a. m. Forty cubic centimeters of serum were injected. Ventricular puncture was repeated at 10 p. m. One cubic centimeter of phenosulphonephthalein was injected intraventricularly in 40 c. c. of serum. Thirty minutes later lumbar puncture was done. A large amount of phthalein was recovered. Sixty cubic centimeters of serum were injected intraspinally.

January 29.—Marked symptomatic improvement. Lumbar puncture gives an almost clear fluid. Forty cubic centimeters of serum were injected. The cerebro-spinal fluid was sterile for the first time on this day.

Lumbar puncture was performed three times subsequently, on January 31, February 2, and February 5. Each time 40 c. c. of serum were injected. The patient showed marked and rapid improvement. On February 5, a marked left facial paralysis appeared and persisted for 10 days. Convalescence was complicated by an acute tonsillitis which appeared on February 9 and lasted six days, and by a typical serum sickness with urticaria and joint pain which appeared on February 16 and lasted three days. The patient was discharged from the hospital on March 17, well. He received a total of 470 c. c. of antimeningococcus serum of which 60 c. c. were given intravenously, 40 c. c. intraventricularly and 370 c. c. intraspinously.

2. (a) Absorption of Drugs Through the Eye. (Abstract.) Dr. D. I. MACHT.

While a large number of drugs are used in eye practice, but few cases of constitutional symptoms due to their systematic absorption are on record, so that some authorities claim that those cases in which systematic symptoms have occurred are to be ascribed to the careless handling of the drugs and their accidental absorption through the mouth. Cases of atropin and cocaine poisoning, however, have been described in which no such explanation is warranted. The following experiments by the author seem to prove conclusively that drugs may be absorbed after instillation into the conjunctival sac more easily than is commonly supposed.

If a few milligrams of apomorphin hydrochloride or a few drops of apomorphin HCl solution (1 per cent) are introduced into the conjunctival sac of a dog, vomiting promptly takes place in one or two minutes. In such an experiment absorption through the mouth by licking is excluded by the experimenter holding the animal still. Inasmuch as dogs react to morphin by vomiting almost as quickly as to apomorphin, exactly the same results were obtained by introducing morphin into the eye. Morphin and apomorphin are emetics which have been proved to exert their effect through a central action on the vomiting center in the medulla. The above experiments, therefore, indicate that these drugs are absorbed through the eye or its appendages. Inasmuch as in addition to the lachrymal apparatus, the vascular and lymph supply of the eye are very highly developed, the author is inclined to believe that absorption takes place not only through the lachrymal and nasal ducts, but also by direct absorption through the blood and lymph.

2. (b) Truth and Poetry Concerning Hydrastis. (Abstract.) Dr. D. I. MACHT.

Hydrastis or golden seal and its alkaloids, hydrastin and hydrastinin, are used interchangeably by medical men for various conditions, especially in the fields of urology and gynecology. Two chief claims have been urged in favor of the crude drug and its alkaloids. On the one hand it has been recommended as a uterine and vesical styptic, and on the other hand as a uterine and vesical sedative. As the action of hydrastis has never been carefully analyzed, the author investigated the pharmacological effects of its principal derivatives, namely, the alkaloids berberin, hydrastin and hydrastinin. It was found that berberin has little physiological effect except when used in very large doses, when it tends to inhibit the contractions of smooth muscle. The effects of hydrastin and hydrastinin were found to be diametrically antagonistic to each other in exactly the same way as those of the opium alkaloids, narcotin and cotarnin, to which they are very closely related chemically. Hydrastinin acts as a stimulant to the smooth muscle of the uterus, urinary bladder and gall-bladder, intestine, vas deferens, bile ducts and blood vessels (isolated and perfused). Hydrastin, on the other hand, inhibits the contractions and relaxes the tonus of all the above-mentioned organs. In tincture hydrastis (alcohol having been removed) the

hydrastin effect generally prevails. From the above experiments it is evident that the sedative effects of hydrastis are chiefly due to hydrastin, whereas the styptic effects of the contractions of blood vessels and the uterus can only be produced by hydrastinin. By choosing the proper alkaloid instead of using the crude drug, the desired therapeutic effect can be produced at the choice of the experimenter.

3. Subacute Streptococcus Endocarditis in the Bacterial and Bacteria-Free Stages. Dr. E. LIBMAN, New York City.

MARCH 19, 1917.

1. The Growth of *Bacillus Coli* in Urine at Varying Hydrogen-ion Concentration. (Abstract.) Dr. A. T. SHOHL and Mr. J. H. JANNEY.

The study was undertaken to determine the effects of accurately measured increases in the acidity and alkalinity on the growth of *B. coli*. As the purpose was to apply ultimately the findings to a study of pyelitis the experiments were done on urine. This was titrated to the desired H-ion concentration by means of colored standards. The standards were phthalates, phosphates and borates; the indicators were methyl red, and the sulphonephthalein indicators. The range covered was from pH 4.0 to pH 9.6. The number of organisms were estimated by diluting and plating on agar and counting the number of colonies. Series were made from the start up to 12 hours.

The results of seven organisms show that *B. coli* has an optimal growth at pH 6.0 to pH 7.0. The acid inhibition point is pH 4.6 to pH 5.0. The alkaline inhibition point is pH 9.2 to pH 9.6.

Typhoid bacilli (Rawlings), streptococci and staphylococci were also used.

2. Acidosis. Dr. L. J. HENDERSON, Harvard University.

MAY 7, 1917.

1. A Summary of End-Results in the Treatment of Cases of Pelvic Abscess by Vaginal Incision and Drainage. Dr. LAWRENCE WHARTON.

2. Observation on the Degeneration of Leucocytes in the Urine as a Diagnostic Aid in Tuberculosis of the Urinary Tract in Women. Dr. H. M. N. WYNNE.

Published in the BULLETIN for August, 1917.

3. Treatment of Leucorrhœa. Dr. H. N. SHAW.

4. A Case of Saphenous Varix Simulating a Femoral Hernia. Dr. E. H. RICHARDSON.

The following case illustrates a condition which appears to enjoy the distinction of having usually led the modern clinical surgeon into diagnostic error. At least, the reported cases, with few exceptions, are confessions of mistaken identity. This one was an arch-offender, having misled and humiliated in succession at least five learned and distinguished surgeons.

Mrs. R. M., white, age 38 years, was admitted to the gynecological department of The Johns Hopkins Hospital on March 4, 1917, complaining of certain symptoms referable to her pelvic organs and of a swelling in the right groin. She had previously undergone two major operations; one four years ago for radical cure of a right femoral hernia and appendectomy, and one in January of this year for a right oblique inguinal hernia. Unfortunately, however, after both operations, when she had convalesced sufficiently to get out of bed the pesky lump promptly reappeared in the right groin. I first saw her on March 7, 1917, a few weeks following her discharge from the hospital after the second operation. The examination disclosed a swelling the size of a hen's egg directly over the femoral canal, which promptly and

completely disappeared in the recumbent posture. A definite impulse and bulging were demonstrable when the patient coughed, but I was unable to recognize either a patent femoral canal or any palpable contents of a hernia sac. The situation of the swelling was particularly interesting in its relationship to the two operative scars, one of which was above Poupart's ligament and the other at least five centimeters below and parallel to it, while the lump appeared midway between them. I made my incision directly over the tumor, but instead of readily exposing a hernia sac, I encountered in the subcutaneous tissues of the groin just over the cribriform fascia and the femoral canal a small circumscribed mass of fatty tissue containing a few lymphatic glands and a plexus of much dilated veins. Both the external abdominal ring and the femoral canal were tightly closed and there were no signs of a hernia present. By withholding the anesthetic and permitting the patient to retch, we were able to positively exclude the existence of a hernia and to observe an enormous distension of the mass of veins. At its lower margin the internal saphenous vein was easily identified and it became obvious that we were dealing with a circumscribed varix of the upper portion of this vein together with its adjacent tributaries. The ligation and division of the trunk veins with excision of the mass of varices and fatty tissue was technically simple. It was interesting to note that there were no varicose veins lower down in the leg. At the time of her discharge from the hospital the patient was apparently cured.

A survey of the literature shows that circumscribed saphenous varix in the region of the femoral canal and external abdominal ring, while uncommon, nevertheless has long been recognized by surgeons as a condition to be differentiated from both inguinal and femoral herniæ. I have collected reports of 10 cases, the earliest being by a French observer, Boinet, in 1836. Seven of these were diagnosed prior to operation either as incarcerated or strangulated femoral hernia.

The condition closely resembles a femoral hernia not only in the size, shape and location of the tumor mass, but also in that it disappears on lying down and imparts a distinct impulse on coughing. The differential points are first, its unusual softness; second, a perceptible thrill which is imparted to the palpating finger when the patient coughs or if slight pressure be made over the mass while the blood escapes from the dilated veins when the patient first lies down; third, having reduced the tumor, if sufficient pressure is made over the femoral canal to prevent the escape of bowel or omentum, and the patient then be allowed to stand up, the tumor will be seen gradually to reform; and finally, the association of varicose veins lower down in the leg is frequent and is a helpful point in diagnosis.

LITERATURE.

1. Boinet. *Gaz. méd. de Par.*, 1836, 2 s. IV, 829.
 2. Camera, U. *Policlin*, Rom., 1912, XIX, 1273.
 3. Coopernail, G. P. *Med. Rec.*, 1914, LXXXV, 1167.
 4. Dawbarn. *Ann. Surg.*, 1900, XXXII, 297.
 5. Brewer. *Ibid.*
 6. Lucas-Championnière (J.). *Assoc. franc. de chir.*, Paris, 1904, XVII, 662.
 7. Noehren, A. H. *Jour. Am. Med. Assn.*, 1910, LV, 2298.
 8. Loos, O. *Beitr. z. klin. chir.*, 1900, XXXVIII, 654.
 9. Segond. Quoted by Loos.
 10. Schwartz. *Rev. gén. de chir. et de thérap.*, Paris, 1915, XXIX, 197.
5. Hematomata of the Ovary Including Corpus Luteum Cysts. DR. EMIL NOVAK.
To appear later in the BULLETIN.
6. Stricture of the Ureter. Report of 100 Cases. DR. H. M. N. WYNNE.
To appear later in the BULLETIN.

MAY 31, 1917.

1. Demonstration of a Simple Method for Determination of Venous Pressure. DR. N. WORTH BROWN.
2. Demonstration of Spontaneous Rhythmic Contraction of Arteries. DR. H. B. RICHARDSON and DR. E. A. PARK.
3. A Hitherto Undescribed Sporotrichum. DR. W. R. SISSON.
4. (a) Studies on Disturbances of Thyroid Function, with Special Reference to Thyroid Adenomata.
4. (b) Adrenalin Hypersensitiveness in Hyperthyroidism. DR. EMIL GOETSCH.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB.

MARCH 12, 1917.

1. Presentation of the Medallion Portrait of Dr. Rupert Norton. Presentation on Behalf of Mrs. Norton by Dr. W. S. Thayer. Acceptance for the Trustees of the Hospital by Hon. Henry D. Harlan. Closing Remarks by Dr. William H. Welch.
Published in full in the BULLETIN for July, 1917.
2. Johns Hopkins and Some of his Contemporaries. DR. HENRY M. HURD.
Published in full in the BULLETIN for July, 1917.
3. Giovanni Maria Lancisi: Clinician, Pathologist, Epidemiologist. (Abstract.) DR. JOHN FOOTE, Washington, D. C.

Giovanni Maria Lancisi was born in Rome in 1654, of middle class parents, who seemed ambitious for their son's career. Giovanni took the usual college course, preparing at first to study theology but later turning to the medical branches. He graduated at the Collegio de Sapienza in 1672 with the degree of doctor. He became an assistant physician at the Santo Spirito Hospital and later accepted a canonship at the church of San Salvatore College, where he studied and taught for five years. He became professor of anatomy in the Collegio de Sapienza in 1684 and taught anatomy for 13 years, becoming at the end of that time professor of the theory and practice of medicine.

While he attended the two preceding popes, he is remembered among the papal physicians especially as the friend and private physician of Clement XI. This pope was of great assistance to Lancisi in his public health work and in financing his various literary undertakings and his teaching.

Lancisi amassed a library of 30,000 volumes which he bequeathed to the Santo Spirito Hospital. This is the first public medical library of which we have any record, excepting some collections of medical books in general libraries. Lancisi died January 31, 1730.

Lancisi was an anatomist, a pathologist, an epidemiologist and a clinician. He was far in advance of his time in his attitude towards questions of public health. He was probably the pioneer European forest conservationist. Unlike many other reformers he did not die in obscurity and unrecognized. He was the friend and correspondent of most of the famous men of his day. He had a singularly useful and happy life, having the time and means to do the work which he loved.

He published and edited the wonderful anatomical plates of Eustachius, which had lain for a century in the Vatican library. In his medical teaching he was an ardent advocate of the clinical method. His interest in pathological anatomy is shown by the numerous autopsy protocols in his writings, especially in his works on "Sudden Death" (1707), and "Aneurisms" (1738).

Lancisi described dilatation of the heart; traced the symptoms which follow it; described various types of vegetations on heart

valves and made the first recorded attempt at a logical classification of heart diseases based on etiology. He differentiated between traumatic and other aneurisms; was the first to advocate percussion over the sternum to determine dullness in the diagnosis of aneurism and was the first to trace the connection between aneurism and syphilis.

His essay on Swamp Emanations and their Cure (1717) will probably be best remembered. In this essay, Lancisi definitely traces the connection between swamp fevers and the mosquito, considers the possibility of infection by the bite of an infected insect causing "worms in the blood," but admits he cannot prove this hypothesis. From the nature of these fevers he is convinced of the connection between mosquitoes and the fevers, and asserts that if swamp emanations are responsible they are and must be organized and living emanations.

His cure, therefore, for swamp fevers is a system of drainage for the swampy lands and other methods including the planting of trees. A translation of portions of this essay as well as a bibliography will appear in the writer's article in *International Clinics*.

4. The Gods of the Underworld in Ancient Medicine. (Abstract.)
(Lantern Slide Exhibit.) DR. F. H. GARRISON, Army Medical Museum, Washington, D. C.

The chthonian deities, of the earth and the underworld, exerted a profound influence upon Greek medicine in the pre-Homeric and pre-Hippocratic periods. The cult is obscure, is but vaguely adumbrated in the classical writers, and what we know of it is the work, not of medical historians, but of archæologists and classical philologists. The main source-book is Rohde's "Psyche." The *locus classicus* for medicine is the passage in the Hippocratic treatise "On the Sacred Disease" assigning the causation of insanity, epilepsy and other neuroses to "the plots of Hecate and the invasion of the Heroes." In the post-neolithic period (Cretan, Mycenaean, Ægean), the chthonian gods were identical with Frazer's "Spirits of the Corn and the Wild," simple divinities of earth and agriculture, who promoted fertility of the soil, prosperity of crops and the general well-being of man. The aboriginal form was the chthonian aspect of the primordial *Magna Mater* or Mother-Goddess of Crete, Egypt and Babylon, who presided over obstetric functions. In the Homeric period, when cremation of the dead was substituted for shaft- and cyst-burial, the entrance of souls into Hades was conditioned by the rite of incineration (often with human sacrifice), the Chthonioi acquired infernal functions, thirsted for the blood of human sacrifice and were feared for their power to wreak evil and inflict disease, in particular the major neuroses. This was also a malignant power of the uncremated dead, who were part of the nightly swarm of evil spirits attending Hecate and Cerberus. Thus Plato (Phædrus, 244) attributes insanity to "ancient wrath" which Rohde interprets as the wrath of the long unburied or uncremated dead. The Greeks were blind to the fact of contagion and put up with the major epidemics as evidences of the wrath of the gods. What they feared were the major neuroses, as these were sometimes inflicted by the Olympian gods also; *e. g.*, in many of the dramas of Euripides, it is highly probable that certain Olympian and chthonian deities were merely identical gods in an uranic or celestial and a chthonic or infernal aspect respectively. Thus medicine in the pre-Hippocratic period was entirely prognostic and prophylactic. Prophylactic medicine was threefold: (1) Apotropaic, designed to *avert* disease by ritual sacrifice or other rites; (2) hilastic, designed to check or abort disease by rites of propitiation or atonement; (3) cathartic, designed to cast out disease invading the body by rites of lustration or purification. The human beings sacrificed in these rites were in time replaced by scapegoats (*Pharmakoi*) in the form of sacred animals and plants, edible, in the case of the Olympian gods, inedible in the case of the chthonian gods. As part of the mystic rite of entering

into communion with the god or of "eating the god," the ritual plants and parts of the ritual animals partaken of by the worshippers at sacrifice came to have supposedly remedial functions. Thus a purely associative ritual therapy arose, which had no pharmaco-dynamic rationale whatever, but was simply based upon the mythologic relation between the god and the plant or animal dedicated to him. This is now true of the major part of the obsolete materia medica of Theophrastus, Dioscorides and Pliny. Max Höfler's tabulation of some 1254 ancient prescriptions of animal remedies goes to show that a part of the body of an animal was seldom employed for a disease of the same part, and even then only as a superstitious rite, since the Greeks knew nothing whatever of the lesions of visceral disease. The Greek scheme of vegetable materia medica was mainly mythological. Greek organotherapy was homœopathic magic, in Frazer's sense, but never real isotherapy in the sense of "like cures like."

LANTERN SLIDES.

1. Aniconic and iconic figurations of the primordial *Magna Mater* or Mother-Goddess (Rhea) of Crete, surmounted by doves in her uranic aspect, attended by lions or entwined with serpents in her chthonic aspect (Sir Arthur Evans). The hieratic attitude of the votary, grasping serpents suggests "Making Medicine" (snake-dance of the Hopi Indians).
2. Babylonian Mother-Goddesses (Yale collections).
3. Christian symbolism of the dove (Rossetti).
4. Demeter chthonia, Kore (Persephone) and Triptolemus (Athenian bas-relief illustrating the Eleusinian mysteries).
5. Conventional Persephone (Rossetti). In her chthonic aspect; Persephone is always styled Kore (The Maiden) in the Greek.
6. Kore (Praxiteles).
7. Antique gems, representing Hermes Psychopompos, the "conductor of souls" (Furtwängler); the soul is represented as a butterfly on the shoulder of Hermes.
8. Eurydice summoned back to Hades by Hermes Psychopompos (Choragic relief at Naples).
9. The Alcestis, Thanatos and Hermes Psychopompos (Relief from the temple of Artemis at Ephesus).
10. Hypnos (Statue by Praxiteles).
11. Hypnos and Thanatos (Drawing by Simeon Solomon).
12. Hypnos and his mother Nux (Night) (Simeon Solomon).
13. Antique gems representing the hilastic rite of *μασχαλισμός* (Æschylus, Choephora, 439, Sophocles, Electra, 445), and the ritual sacrifice of a maiden for apotropaic purposes (Furtwängler).
- 14-18. Five stages in the progress of the Æsculapian tradition:
 - (a) Æsculapius in his aboriginal chthonic aspect as an ancient Thessalian earth- or cave-god, the *genius loci* of healing springs, shrines and temples, usually appearing as a serpent (*agathos daimon*) (Rohde).
 - (b) Æsculapius in the Homeric tradition as a mortal hero-physician of Thessaly, whose sons acted as naval and military surgeons in the Trojan war (Catalogue of the Ships).
 - (c) Æsculapius in the Pindaric tradition as a demi-god, the son of Apollo. Deified by a thunderbolt of Zeus, he assumes the celestial (uranic) aspect of the latter.
 - (d) Æsculapius in the later Greek tradition as a heroized physician (Heros Iatros), with a temple (Heroön) of his own near the Theseion at Athens (Demosthenes). Having assumed his mortal aspect again, his "grave" is shown in various places, and his descendants, the Asclepiads, have separate shrines of their own (Rohde).
 - (e) Æsculapius in the later Roman tradition reassumes his primordial chthonic aspect. He ends, as he began, as a serpent (Pliny, Nat. Hist. XXIX, 22; Ovid, Met. XV, 626-744).
- 19-30. Slides showing the serene, philosophic attitude of the ancients toward death as contrasted with the morbid mediæval view. In antiquity, the skeleton, when figured on gems or wine-

cups, was only a quizzical *memento mori*, the "skeleton at the feast" (Parkes Weber). In the Middle Ages and the Renaissance, it became the conventional sign and symbol of Death as the King of Terrors. The mediæval painters copied the spectral aspect (*Lemurengestalt*) of the eviscerated corpses and the dried skin-and-bone skeletal preparations (*Hautskelett*) in the MS. anatomical drawings (Sudhoff). The skeletons and eviscerated figure in The Books of Hours suggest that these were probably derived, in the first instance, from MS. anatomical illustrations by dissectors rather than from the imagination of the decorative artists. The Spanish painters represented royalties and great ladies as decomposing in their coffins. Rossetti's Beata Beatrix, an evocation of his dead wife, is un-English in conception. The feeling is mediæval Italian, that of Dante's *Vita Nuova*. The figure at the Adams tomb by St. Gaudens, in the cemetery in Rock Creek Park, D. C., according to the sculptor's intention, symbolizes Nirvana, the immobility or immobilization of the Orient.

THE LAENNEC SOCIETY.

MARCH 26, 1917.

X-Rays in Tuberculosis.

1. The Roentgen Diagnosis of Pulmonary Tuberculosis. DR. HENRY K. PANCOAST, Philadelphia, Pa.
2. A Comparative Analysis of Roentgen Ray Pictures, Physical Signs and Symptoms in Pulmonary Tuberculosis. DR. F. H. HEISE and MR. H. L. SAMPSON, Saranac Lake, N. Y.

DISCUSSION.

DR. F. H. BAETJER: I was glad to hear two notes sounded in the right terms in both these papers. The first, conservatism, and the second a note of cooperation. As one travels around the country and goes to a great many roentgenological laboratories, one is struck with the absolutely flat-footed diagnosis of tuberculosis from roentgenograms. My own feeling is that that is a mistake. We class tuberculosis down here as roentgenological tuberculosis and clinical tuberculosis. Roentgenological tuberculosis is, of course, of great interest to us, and clinical tuberculosis to the patient.

We know that in nearly all autopsies, if we look for it carefully, we find evidence of tuberculosis. If we have got evidence of tuberculosis from the anatomical standpoint, are we not going to get evidence in our plates? The question comes up, Is this tuberculosis we see in a plate of any significance as far as the patient is concerned? We frequently see coming up either from the wards or from the dispensary, lungs which in one sense might be termed fairly well shot to pieces by tuberculosis, although the patients may not have any temperature, may be doing their work, up and about. Now because we have found tuberculosis there, to say that that patient must go away and be treated would, of course, be an obvious error. In other words, it seems to me that tuberculosis is a clinical disease absolutely.

The roentgenogram can play a very important part in tuberculosis, as has been pointed out by the two speakers to-night. In the first place we can detect early permanent changes sooner than the clinician can. Understand me, I say permanent changes, not saying anything about the etiological factor in early incipient tuberculosis. I do not believe we are able to make a positive diagnosis. Of course the great difficulty is that the term incipient tuberculosis is used in different ways in different places. Quite recently a patient was referred to the roentgenological department, where we found consolidation and one or two small cavities in the right upper lobe. This case had been treated at a sana-

torium here and came down with a diagnosis of incipient tuberculosis. The X-Ray was not needed in this case for diagnosis.

I do not believe we can make an etiological diagnosis in the earlier cases. If there are permanent changes, however, I believe the X-Rays are of value in pointing this out and we may suggest that we think it is tuberculosis. Tuberculosis does reach a stage when we can say "This is tuberculosis," but when that stage is reached the clinician does not need us to help him to make a diagnosis.

In regard to the question of chronicity and acuteness, the greater the amount of fibrous tissue we see in a lung means chronicity, and the greater involvement without fibrous increase means a more or less acute condition. The great difficulty is where we have a fibrous change with a flare-up on top of that. Can we tell anything about that? Personally, I do not think we can.

The other point the speakers to-night brought out is the question of cooperation. After all, what we are working for is the benefit of the patient and not to get something on the clinician or the roentgenologist. It is only by cooperation that we are going to get the very best results.

I should like to ask Dr. Heise something further in regard to his statement that in 17 per cent of his cases they found signs which were not found in the roentgenogram. Some time ago a number of students, presumably normal, were examined both clinically and from the roentgenological standpoint, Dr. Hamman, of course, making the clinical examination. Very careful notes were made and the field was limited almost entirely to the apices, because we thought the clinician has best opportunity there to detect small changes. It was quite interesting to note the agreement and disagreement. In some cases we agreed absolutely, and in others disagreed as to whether the change was in the right or left apex. The notes would read something like this: "Note on the right side possibly a little more blowing or high pitched." From these conclusions, one would say that the right side was involved and the left normal, although from a roentgenological standpoint we would sometimes find just the reverse. In other words, the physician would be at a loss to determine which of these two sides was normal, as he would have to depend entirely upon the comparison of the notes. In just such cases the roentgenogram would indicate which was the normal and which was the affected side.

DR. LOUIS HAMMAN: Fifteen years ago sanatorium physicians taught us that the results of treatment in pulmonary tuberculosis depended primarily upon the stage of the disease when treatment is begun. Under the influence of their indubitable demonstration clinicians have eagerly sought for aids to reach a definite diagnosis at the very earliest stage of the disease. Tuberculin for a time was vaunted as the sovereign means with which to reach an indisputable conclusion. Larger experience and critical analysis has not substantiated this extravagant claim for tuberculin. Later it was hoped that extreme finesse in percussion and auscultation would supply the necessary criteria. These arts have also failed us as conclusive arbiters. At the present time the enviable position left vacant by the failure of tuberculin and of percussion and auscultation to measure up to expectations is usurped by the roentgen ray. In many quarters roentgenograms or fluoroscopic pictures of the lungs are regarded as superior substitutes for the humbler methods of physical exploration, and some devotees of this branch of medicine are satisfied to settle all disputed questions upon the evidence of their art irrespective of other clinical data. This statement is daily illustrated in practice, for it is a common experience to have patients apply for a verification of the diagnosis of pulmonary tuberculosis when this diagnosis rests solely upon roentgenographic studies. We are all familiar with the judicious and conservative attitude taken towards this question by Dr. Baetjer, and it is very gratifying to learn that such prominent

investigators as are our visitors have come to similarly conservative conclusions. Expressions of opinion from these authorities will do much to check harmful exaggeration of the importance of the roentgen ray in the early diagnosis of pulmonary tuberculosis.

DR. HEISE: In regard to Dr. Baetjer's question, I would say that the changes were mainly those of breath sounds without râles. In one or two instances there were râles at the base.

APRIL 30, 1917.

Tuberculosis as a Social Problem.

1. **The Public Health Work of a Great Life Insurance Company.**
DR. HORACE JOHN HOWK, Mt. McGregor, N. Y.
2. **The Social Service Side of Tuberculosis Work in New York.**
DR. JAMES ALEXANDER MILLER, New York City.

BOOKS RECEIVED.

Care of Patients Undergoing Gynecologic and Abdominal Procedures Before, During and After Operation. By E. E. Montgomery, A. M., M. D., LL. D., F. A. C. S. Illustrated. 1916. 12°. 149 pages. W. B. Saunders Company, Philadelphia and London.

Focal Infection. The Lane Medical Lectures. By Frank Billings, Sc. D. (Harv.), M. D. Delivered on September 20, 21, 22, 23 and 24, 1915, Stanford University Medical School, San Francisco, California. 1916. 8°. 166 pages. D. Appleton & Co., New York and London.

A Manual of Nervous Diseases. By Irving J. Spear, M. D. With 172 illustrations. 1916. 16°. 660 pages. W. B. Saunders Company, Philadelphia and London.

A Treatise on Diseases of the Skin. For Advanced Students and Practitioners. By Henry W. Stelwagon, M. D., Ph. D. Eighth edition revised. With 356 text-illustrations and 33 colored and half-tone plates. 1916. 8°. 1309 pages. W. B. Saunders Company, Philadelphia and London.

The Diagnosis and Treatment of Abnormalities of Myocardial Function. With Special Reference to the Use of Graphic Methods. By T. Stuart Hart, A. M., M. D. Illustrated with 248 Engravings, 240 of which are original. 1917. 8°. 320 pages. The Rebman Company, New York.

The Clinical Diagnosis of Internal Diseases. In three volumes. By Lewellys F. Barker, M. D. (Tor.), LL. D. (Queens; McGill). Volume I (Parts I-VI) *General Diagnosis, Infections, Respiratory and Circulatory Systems.* Volume II (Parts VII-X) *The Blood, Digestive System and Urology.* Volume III (Parts XI-XIV) *Muscles, Bones and Joints, Nervous System, Metabolism.* 1916. 8°. D. Appleton & Co., New York and London.

The Harvey Lectures. Delivered under the auspices of the Harvey Society of New York, 1914-1915. By Prof. Frederick P. Gay, Dr. Thomas Lewis, F. R. C. P., Prof. A. S. Loevenhart, and others. Series X. 1915. 8°. 339 pages. J. B. Lippincott Company, Philadelphia and London.

AN APPEAL TO THE MEDICAL PROFESSION OF THE UNITED STATES.

The Surgeon General's Office has appealed to the medical press of this country for aid in securing the quota of physicians necessary for the care of the great army now in course of organization.

The Medical Departments of the Government are responsible for the examination of the recruits, the hygiene of camps and the care of the sick and wounded. The Surgeons General have not as yet been given full authority and the means to meet this responsibility.

The President and Congress can give the Surgeons General full authority and ample means, but except by the draft neither the President nor Congress is able to give them a sufficient number of men from the medical profession, as it is a volunteer service. Consequently, if the Medical Departments are furnished with the authority and the means, they will still be unable to do their work unless the medical profession of the country, and particularly the younger men, respond more freely than they have done up to this time.

In the army hospitals and first aid work abroad, in the vast concentration camps so soon to be organized in this country, and in every branch of the naval service there is an urgent demand for each physician who can and will offer his services. In the work our country has pledged itself to do, the need for doctors is imperative. Estimates give the figure of 20,000

physicians as the minimum number necessary for this work. Only about 6000 are at present enrolled. These figures speak for themselves.

Commissions in the Medical Reserve Corps are accorded on the basis of First Lieutenant, Captain and Major, with respective salaries of \$2000, \$2400 and \$3000 a year. Applicants may apply directly to the various examining boards throughout the different states and complete all preliminary arrangements without reference to the Surgeon General's Office. The completed papers should be forwarded directly to the Surgeon General by the president of the examining board. A complete set of papers must contain the physical examination, report of the examiner as to mental, moral and physical qualifications, a personal history form filled out by the applicant and sworn to before a notary, and a certificate of state registration (except where this year's graduates have not had time to take their State Board examination). Two letters should also be sent certifying as to citizenship and moral qualifications, and, if of alien birth, a certificate of naturalization.

Further information may be obtained from the State and County Committees of National Defense, or directly from Surgeon General W. C. Gorgas, of the Army, or Surgeon General W. C. Braisted, of the Navy, Washington, D. C.

BULLETIN

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A HISTOLOGICAL STUDY OF 50 UTERI REMOVED AT CÆSAREAN SECTION.*

By J. WHITRIDGE WILLIAMS,

Professor of Obstetrics, Johns Hopkins University and Obstetrician-in-Chief to The Johns Hopkins Hospital.

During the past 20 years we have had occasion in my service to amputate the body of the uterus supravaginally and to treat the stump extraperitoneally in 50 cases following delivery by Cæsarean section. In each instance the specimen has been preserved and subjected to careful histological examination.

The study of this comparatively large material has yielded important information concerning a number of questions; more particularly concerning the mechanism of the separation of the placenta and of the foetal membranes; the amount of decidua retained immediately post partum; the vascular changes at the placental site; the retraction of the uterine muscle; the occurrence of ascending infection in patients who had been long in labor, or who had been repeatedly examined by persons neglecting rigorous hand disinfection; and finally concerning the characteristics of the cicatrix resulting from previous sections, and its bearing upon the correctness of the dictum—"Once a Cæsarean always a Cæsarean."

I have thought that a brief analysis of my findings might prove of interest, more particularly as they are not in accord with certain current teachings, and as they show that many of the statements concerning the third stage of labor contained in the text-books are too arbitrary and general.

At first glance, it might appear that we have been too liberal in the indications for the performance of an operation, which necessarily puts an end to the reproductive process; but, although I am prepared to admit the justice of the criticism for a small number of cases, I contend that impartial study of the indications will show that our practice has been generally conservative. In view of my experience that the convalescence following this operation is more satisfactory than that following the classical section, except when done at an appointed time at the end of pregnancy or at the very onset of labor, we have in the past employed it in cases in which we would now resort to pubiotomy or extra-peritoneal Cæsarean section. Furthermore, until very recently, we have employed it as the operation of choice in all cases in which it was thought advisable to prevent further conception. Accordingly, we have

* Read in abstract, with lantern demonstration, before the American Gynecological Society, June, 1917.

resorted to it in many patients who required a second or third Cæsarean section, as well as in those suffering from serious heart lesions, in whom a repetition of pregnancy bid fair to put the patient's life in serious jeopardy. Finally, we have employed it in certain feeble-minded or profoundly deformed individuals in whom repeated pregnancy seemed undesirable from an economic or social point of view.

At present, in these latter types of cases we bring about sterility by double ligation and section of the tubes followed by the burial of their proximal ends between the folds of the broad ligaments, and restrict the use of supravaginal amputation to frankly infected cases and to those presenting definite uterine lesions.

Analysis of our series of cases shows that the operation was undertaken for the following indications:

	Cases.
Repeated Cæsarean sections	10
Frank infection	8
Rupture of uterus	5
Serious heart lesions	4
Atresia of cervix	3
Intramuscular hæmorrhage associated with premature separation of the placenta.....	2
Myoma of the uterus	2
Atonic hæmorrhage	2
Pregnancy in a rudimentary horn	1

a total of 37 cases, leaving a balance of 13 cases in which the operation was undertaken for various other indications. Looking backwards, I acknowledge that supravaginal amputation may have been unnecessary in a small number of the latter group of cases, but for the great majority I contend that it was a fully justifiable procedure.

Before taking up the analysis of the histological findings in our series of specimens, a few words concerning the structure of the pregnant uterus at term, of the placenta, and of the membranes outside of the placental site, will make it easier to understand the changes occurring during the third stage of labor.

Fig. 1, which represents the left half of the uterus of a woman who died from eclampsia, without convulsions, prior to the onset of labor, shows the tightly contracted empty bladder, a portion of the vagina and the unchanged cervix. Its most instructive portion, however, is the body of the uterus, with the placenta attached to its upper and anterior portion. The uterine walls were tightly contracted over their contents, as is shown by the impression of a foot of the child upon the internal surface of the placenta. Outside of the placental site the interior of the uterus is lined by the foetal membranes; and except at one point on the posterior wall, the most surprising feature is the extreme thinness of the uterine walls, which including the foetal membranes and decidua vary in thickness from 1.5 mm. in the lower uterine segment to 3 or 4 mm. at the placental site. This is in marked contrast to the conditions existing in the non-pregnant organ and during the first half of pregnancy. In the latter condition, the uterine walls are thick, and the decidua vera measures from 7 to 10 mm. in thickness and presents its characteristic compact and spongy

layers. It is apparent that the present conditions can have resulted only from pronounced distention of the uterus by its contents, with consequent thinning of its walls, and therefore one cannot expect to find either the muscle wall or the decidua presenting the same structure as in early pregnancy.

Fig. 2, which represents a section through the wall of a full-term pregnant uterus outside of the placental site, clearly illustrates these points. In the first place, it is seen that the muscularis has in great part lost its felt-like structure and that its fibers are arranged in almost parallel strands. In the second place, it is seen that the fused decidua vera and capsularis, together with the foetal membranes, form a layer of about 1 mm. in thickness, two thirds of which belong to the former and one-third to the latter. The decidua in great part consists of the compact layer and contains only a few glands. This, however, is not a general rule, as in other specimens this relation may be reversed, when the bulk of the decidua will consist of the spongy layer. The essential point is the relative thinness of the decidual layer, and the fact that it differs greatly from the condition usually described as typical, so that when separation occurs during the third stage of labor it will not always be easy to determine whether it has taken place in the compact or in the spongy layer.

Furthermore, it will be noticed that the junction between the outermost portion of the decidua and the muscularis forms an almost straight line, instead of the serrated junction characteristic of the early months—a point to which Aschoff directed attention in 1899.

When we pass to the placental site, it is apparent that the comparatively thick decidua basalis of the early months has likewise undergone a radical change, and, although it may be thicker than the decidua vera, it rarely exceeds a few millimeters in thickness and may be much thinner. Indeed, no general rule can be laid down in this regard, as it may happen in the same placental site that in places the basalis may be relatively thick and in others almost completely lacking.

Figs. 3 and 4, from other full-term pregnant uteri, clearly illustrate these differences. In the former the basalis is quite thin, contains no glands and is made up of a few layers of partially degenerated decidual cells, interspersed with large foetal cells possessing deeply staining nuclei. In the latter it is seen that the basalis is sharply differentiated into a compact and spongy layer, and that the latter makes up the greater part of its thickness. It is also seen that the epithelium lining the glands in the deepest part of the spongy layer is well preserved, and is apparently ready to effect the regeneration of the endometrium during the puerperium.

Fig. 5, represents a section through another pregnant uterus at term. In its upper portion it illustrates the foetal portion of the placenta, with amnion, chorionic membrane, and villi; while in its lower portion it represents the decidua basalis with a trophoblastic or, as it was formerly designated, a decidual septum projecting up into the intervillous space. In this specimen, to the sides of the septum, the decidua basalis is unusually thin and consists almost entirely of so-called fibrinoid or canalized fibrin.

From the study of these three sections, it is apparent that the decidua basalis varies greatly in structure, and consequently it is not justifiable to lay down the general rule that separation during the third stage of labor must take place in the spongy layer. At any rate, such a mechanism would be out of the question in the specimens represented by Figs. 3 and 5, in which a spongy layer was entirely lacking.

Location of placenta.—Passing to the study of our 50 specimens, the first point to claim our attention is the location of the placental site, and our statistics show that the placenta was attached to the anterior wall of the uterus in 18 and to the posterior wall in 32 instances. In 15 of the 50 specimens, the placenta remained firmly attached to the uterine wall after the completion of the operation, while in the other 35 cases it had either separated spontaneously or had been removed manually before amputation of the organ.

In the cases of retention, the placenta was attached to the anterior wall in three and to the posterior wall in 12 instances. The lesser incidence of the attachment to the anterior wall in this group of specimens, as contrasted with those in which separation had occurred, is probably attributable to the fact that when implanted anteriorly it was necessary to incise or to separate the placenta manually before delivering the child.

Uterus Immediately Post Partum.—Immediately after the extraction of the child by Cæsarean section, the uterus with the placenta still *in situ* is delivered through the abdominal wound, and the peritoneal cavity is protected with sterile gauze pads. At this time, the uterus has contracted tightly down upon its contents, and the hæmorrhage is usually minimal. The various procedures preliminary to amputation are now undertaken, and in many instances, while they are in progress, the placenta is spontaneously extruded. In other cases such profuse hæmorrhage may follow its partial separation that manual removal becomes necessary in order to permit the uterus to contract with sufficient force to control the bleeding, but in 15 of the specimens, as has already been mentioned, the placenta and membranes remained *in situ* at the end of the operation.

Consequently, the condition of the uterus will vary according as the placenta has been expelled or not. In the former case the body of the uterus is represented by an almost solid mass of muscle including in its interior the almost completely obliterated cavity, and measures on the average 16 cm. in length, 12 cm. in breadth and 8 cm. in thickness. In other words, the thin-walled muscular sac depicted in Fig. 1, has become transformed into a structure whose walls average 3.5 to 4 cm. in thickness. Strange to say, in this group of specimens, particularly when hardened, it is frequently impossible to identify the placental site with the naked eye, and its location can be determined only after microscopical examination.

In the specimens in which the placenta remains *in situ*, the body of the uterus is still larger, and the comparison of Fig. 1 with Fig. 6, which represents a sagittal mesial section through such a specimen, after hardening, gives a graphic picture of the changes that have occurred. In the first place the thin-walled full-term pregnant uterus has become dimin-

ished by about one half in length and thickness and converted into a thick-walled structure, whose cavity is completely occupied by the placenta and the foetal membranes. The muscular walls have increased to 2.5 to 3 cm. in thickness, while the uterine cavity has become diminished from a huge space to a mere slit between the free surface of the placenta and the anterior uterine wall. At the same time the area of placental attachment has decreased nearly one half in length, while the placenta has increased several times in thickness. Furthermore, the foetal membranes have been transformed from a structure but little thicker than a sheet of paper into a layer several millimeters thick, which presents a wrinkled appearance and upon closer inspection is seen to be made up of myriads of minute wavy folds or festoons.

In several instances, in which the placenta was inserted upon the posterior wall of the uterus with its upper margin extending well into the fundal region, another phenomenon was observed: namely, the posterior wall, with the placenta still attached, became inverted through the uterine incision. That this was the result of uterine retraction was clearly demonstrated by the fact that on one occasion I observed the same phenomenon follow the sudden contraction of the still warm uterus incident to its immersion in a 10-per-cent solution of formalin.

The consideration of the histological conditions obtaining in the empty uterus will be deferred until later, and we shall now turn to those observed in uteri in which the placenta is still *in situ*. In all of the 15 specimens belonging in this category the placental site had undergone a definite decrease in size, whence it would naturally be inferred that the decidua basalis must have undergone a corresponding thickening. Doubtless, this did occur, but the study of our specimens indicate that it is much less extensive than might have been expected, and still further confirms the statements made above concerning the varying structure of that membrane. Designating the decidua basalis as thick or thin according as it equals or exceeds 2 mm., or measures less than 1 mm., respectively, our figures give the following data: decidua basalis, thick, two cases, thin, seven cases, varying, five cases, and lacking, one case.

The last observation (Specimen No. 713) is of particular interest, as in it the chorionic villi were either attached directly to the muscularis or were separated from it by a very thin layer of canalized fibrin containing a few isolated decidual cells. But in any event, the classical compact and spongy layers were lacking and, had separation occurred, it could not have been described as following the mechanism usually outlined in the text-books.

As has already been mentioned, in all of the specimens in which the placenta remained *in situ*, as well as in a number in which it had been expelled, but in which a portion of the membranes had been retained, the interior of the uterus was lined by a layer of tissue several millimeters thick, which instead of presenting the smooth glistening appearance of the distended amnion offered a dull corrugated surface, which upon closer examination was found to be due to the presence of myriads of minute folds or projections.

Upon microscopic examination it becomes apparent that this appearance is due to the fact that the decidua vera and the chorion laeve had been thrown into delicate waves or festoons, while the amnion, unable to accommodate itself to the process, had become puckered, with the result that its free surface was converted into innumerable papillary excrescences of varying size.

Figs. 7 and 8 give an excellent idea of these changes and offer a marked contrast to the conditions present in the undelivered uterus at term, as shown in Fig. 2.

Careful study of such sections show that the bulk of the decidua vera is contained in the interior of the festoons, and that only a relatively small portion remains in contact with the muscularis; and furthermore, that its line of junction with the latter has become wavy or serrated, so that in many places small triangular masses of decidual tissue, containing well-preserved gland spaces, project down into the interstices between the muscle bundles. In other words, the mutual relation between the two structures has been restored to that which existed in the early months of pregnancy, and which had disappeared with the increasing distention of the pregnant uterus. Processes of chorionic connective tissue covered by many layers of chorionic epithelium, in which remnants of atrophic villi are sometimes visible, project down between the decidual folds and are firmly united to them.

This festooning of the foetal membranes and the decidua was noted by Dohrn in 1865 and by Ahlfeld in 1881, but was first thoroughly described by Barbour in 1884, whose article was accompanied by excellent colored illustrations. Since then it has been mentioned by various writers, among whom Champneys, Krönig, Keilmann and Gessner may be mentioned. Accordingly, although this observation is not new, I do not think that its significance has been sufficiently appreciated, either on account of its scientific interest or because of its bearing upon the mechanism of the separation of the membranes.

Of course its mode of production is perfectly apparent, and represents nature's method of temporarily adjusting the large superficies of the interior of the full-term pregnant uterus to the restricted area available in the freshly delivered organ. Its bearing, however, upon the mechanism of separation of the membranes, and the regeneration of the endometrium post partum is of prime importance. From a study of the illustrations, it is evident that separation can occur only at the basal ends of the festoons, and that as many of them reach almost to the muscularis and as the bulk of the decidua vera is included between them, only a minimal amount of decidua will ordinarily be left *in utero*. In these circumstances, therefore, separation must usually occur in the deepest layers of the spongy layer, so that the triangular areas of decidual tissue included between the muscle bundles must play a very prominent part in the process of post-partum regeneration.

Corresponding to the diminution in size of the maternal aspect of the placenta, the amnion covering its foetal surface is frequently thrown into folds, similar to those occurring in the membranes. The chorionic membrane, however, does not

take part in the process, and continues to present a smooth foetal surface.

Mechanism of Separation of the Placenta and Membranes.
—As early as 1881, Ahlfeld attempted to study this problem upon the basis of the findings in a uterus removed by Dohrn at a Porro Cæsarean section. As in his specimen the uterine cavity was obliterated and the placenta still firmly attached, he concluded that retroplacental hæmorrhage was not the essential factor in inaugurating the separation of the organ, and he therefore attributed it to the inability of the maternal surface of the placenta to accommodate itself to the constantly decreasing area of the placental site.

Opposition to his teachings immediately developed, and Sängér, Leopold, Kerr and others contended that such pronounced alterations in the action of the uterus must result from the presence of the incision in its anterior wall that it would be inadmissible to assume that phenomena following Cæsarean section, no matter whether the uterus was retained or removed, would necessarily apply to the normal unopened organ.

Barbour and Hart did not share this view, but contended that such observations threw a flood of light upon the normal mechanism of the separation of the placenta. They, as well as Schroeder, Stratz, Nyhoff, and others, held that separation did not normally occur during the contractions of the first and second stages of labor, for the reason that the placenta was firmly pressed against its site of attachment by the general intrauterine pressure, and furthermore, that the moderate diminution in area of the placental site was compensated for by a corresponding decrease in size of the placenta, which was brought about by a part of the contents of the vessels in the chorionic villi being mechanically squeezed into the general foetal circulation. In the third stage of labor, on the other hand, these factors no longer come into play, and the lack of correspondence between the placenta and its area of attachment becomes greatly accentuated. Barbour contended that this only prepared the way for separation, but that the process was not inaugurated until alternating contraction and relaxation occurred later. Consequently, he attributed the separation to uterine activity, and believed that retroplacental bleeding was only a secondary factor. Hart expressed himself more or less paradoxically, and stated that separation was less the result of diminution in the area of the placental site than of a relative enlargement of the placenta, which resulted from the inability of the vessels of the chorionic villi to rid themselves of their contents.

While I am prepared to admit, at least in part, the justice of the contentions of those who claim that incision and manipulation of the uterus introduce a disturbing factor into the physiology of the third stage of labor, I nevertheless feel that our series of specimens—and particularly those in which the placenta remained *in situ*—give important clues concerning the mechanism of separation.

In the first place, they clearly demonstrate the diminution in the area of the placental site, and show that the placenta, in order to accommodate itself to the process, has increased

markedly in thickness. In the second place, the fact that in nearly one third of the specimens the placenta was still *in situ* and showed no sign of separation or of hæmorrhage beneath it, during the 10 or 15 minutes which had elapsed between the delivery of the child and the amputation of the uterus, clearly demonstrates that retroplacental hæmorrhage does not always appear promptly, and to some extent justifies the assumption that it is not usually the primary factor concerned, but develops secondarily after some other mechanism has inaugurated the separation.

In the third place, the festooning of the foetal membranes and the decidua gives conclusive information concerning the mechanism of their separation; as it is apparent that the way has been prepared for their detachment by traction or gravity as soon as the placenta has become loosened from its attachment and begins to descend.

On the other hand, our specimens give no information concerning the immediate cause of separation of the placenta, and force us to take refuge in hypotheses if we wish to attempt to explain the entire mechanism of the process. Figure 9, which represents a section through a uterus in which the placenta was partially adherent, shows very clearly the line of cleavage in the decidua basalis, and the relative amounts of it which are cast off with the placenta and retained *in utero*, respectively. Furthermore, the relatively small size of the space between the two layers indicates that the amount of retroplacental bleeding has been minimal.

Location of Separation of Placenta and Membranes.—Although Matthews Duncan, in 1868, had given an extensive historical résumé of the work done upon this subject, in which he pointed out the fallacy of the older view that the entire mucosa was cast off at the time of labor and showed that considerable portions of it were normally retained and served for the regeneration of the new endometrium, it was not until after the appearance, in 1870, of Friedländer's classical work upon the structure of the decidua that interest in the question became acute. As is well known, this writer gave an accurate description of its histological structure, and established the differentiation between the compact layer adjoining the uterine cavity and the spongy layer adjoining the muscularis. He also stated that at the time of labor separation normally occurred in the deeper portion of the compact layer, so that a thin remnant of it as well as the entire spongy layer was retained.

This doctrine remained uncontradicted for five years, when Langhans stated that it was quite erroneous, and that the line of cleavage normally occurred in the spongy layer, so that only the fundi of the glands were retained and were available for the regeneration of the endometrium. As the extensive work of Kundrat and Engelmann and of Leopold upon the structure of the endometrium in its various phases was published about the same time and confirmed Langhans' views, it has been generally accepted that separation normally occurs in the spongy layer, and this teaching has been incorporated into the text-books.

Friedländer did not allow Langhans' teachings to go unchallenged, and in 1878, reiterated his original view, at the same time giving a description of a specimen in which the entire decidua had been retained after the extrusion of the placenta. Various other writers took a more conservative position; thus, Küstner and Fehling held that cleavage might occur in either layer, and Caratulo stated that it occurred in the spongy layer at the placental site and in either the compact or spongy layer elsewhere in the uterus. Barbour, on the other hand, believed that the significance of the spongy layer had been greatly exaggerated, while Krönig, in 1901, expressed surprise at finding how little decidual tissue was normally retained.

In view of these contradictory statements, the findings in our series of specimens may be of interest. As has already been gathered from the description of the placenta and membranes before delivery, it is apparent that uniform conditions do not always obtain and that the structure of the decidua basalis and vera at term differ so markedly from those existing in the early months of pregnancy that it is to be assumed that the conditions found immediately post partum would not correspond with those postulated by the assumption that Friedländer's classical description of the structure of the decidua persists throughout the entire duration of pregnancy.

Our findings fully bear out these *à priori* deductions, as 40 of our specimens are available for solving the question. They show that separation had occurred entirely in the compact or in the spongy layer in 7 and 28 instances, respectively; while in five other instances the separation was irregular, occurring in some areas in the compact and in others in the spongy layer.

Still more definite conclusions may be deduced from the study of the 35 specimens in which the placenta and membranes had separated before amputation of the uterus. Thus, sections through the placental site show that the portion of decidua retained could be designated as thick in 10 and as thin in 10 other specimens. In an additional instance no trace of decidua could be found, while in the remaining 14 specimens the amount retained varied, being thick in some places and thin in others, and entirely lacking in still others, except for the minimal amounts contained in the triangular areas extending down between the fibers of the retracted muscularis.

Fig. 10, gives a good idea of the conditions obtaining when cleavage has occurred in the compact layer, and the poor preservation of the glandular epithelium, except in the immediate vicinity of the muscularis, makes it evident that everything above it will probably be cast off in the lochia before the process of regeneration is inaugurated. Figures 11 and 12, which are diagrams from sections through different portions of the placental site of another uterus, give a clear idea of the varying amounts of decidua basalis which may be retained in the same organ. Furthermore, sections outside of the placental site show that analogous variations occur in the decidua vera. Thus, the retained portion was found to be thick in 11, thin in 7 and of varying thickness in 17 instances.

In other words, our study shows that hard and fast rules cannot be laid down concerning the line of cleavage during

the third stage of labor or, as to the amount of decidua which will be retained at the placental site or elsewhere in the uterus. In some cases cleavage occurs definitely in the spongy layer, less frequently in the compact layer, but very often it is irregular, involving the spongy layer in some places and the compact layer in others. Consequently, the amount of decidua retained may vary greatly in different specimens, and all gradations may be observed varying from a thick layer on the one hand to minute decidual triangles between the serrated margin of the muscularis on the other.

Placental Site.—The structure of the decidua basalis both before and after the separation of the placenta has already been studied, but several histological points of interest in this area remain to be considered—particularly the occurrence of foetal cells and certain vascular changes.

In a previous section of this report reference was made to the fact that in not a few specimens it was impossible to locate the placental site macroscopically, and that its location could only be established after microscopical study. In such cases neither the amount of decidual tissue retained nor the increased vascularity enables one to make a decision, which in our experience depends almost entirely upon the recognition of foetal-cell infiltration or of certain vascular changes, which only occur in this locality.

As early as 1865 Dohrn described in the decidual basalis the presence of large cells with deeply staining nuclei which stood out in marked contrast against the typical decidual cells. Friedländer and Leopold observed similar structures, which the latter described as decidual giant cells, and held that their active invasion of the vessels played a causal part in the production of the thrombosis, which he believed was essential to the onset of labor and to the prevention of post-partum hæmorrhage.

Since then these cells have been studied by numerous investigators, among whom Pels-Leusden, Winkler, Pinto, Aschoff and Schickele may be mentioned. They vary greatly in size and shape, but possess the common feature that their nuclei contain an abundant chromatic network which stains deeply with various reagents. The cells may be spindle-shaped, round, polygonal or irregular in outline and sometimes contain several nuclei. They occur only at the placental site, but are not limited to the decidua basalis, as they may extend far down into the muscularis, usually in connection with strands of connective tissue accompanying the blood-vessels. They begin to appear in the early weeks of pregnancy, attain their maximum development somewhere between the fourth and fifth months, usually persist throughout the balance of pregnancy, and disappear during the first week of the puerperium.

It would lead too far afield to consider their history and significance, and it must suffice to say that, while Pels-Leusden, Winkler, Pinto and others hold that they are maternal in origin, the great majority of authorities consider that they are wandering foetal cells derived from the chorionic epithelium, in which opinion I concur.

Such foetal cells were present in the placental site in 35 of our 50 specimens, and in a number of instances, as has already

been indicated, were the principal factor in leading to its identification. Their presence in 70 per cent of our specimens effectively disposes of the statement of those authors, who contend that they disappear normally before full term is reached.

As has already been indicated, Friedländer, and more particularly Leopold, directed attention to the invasion of venous channels in the placental site by the so-called decidual giant cells. They held that the process originated in the later days of pregnancy, and was the main factor concerned in the production of thrombosis, which they believed played an important part in the causation of labor and particularly in the prevention of hæmorrhage after the extrusion of the placenta. Since then the regular occurrence of such thromboses has been generally accepted and taught.

The study of our specimens, however, has shown that such teachings are erroneous, and while thrombosed vessels can always be found at the placental site of women dying during the puerperium they are usually lacking in freshly delivered uteri. Our statistics show that they were present in 11 of our 50 specimens, but in every instance the thrombi were fresh, merely consisted of recently clotted blood, and showed no evidence of organization. Consequently, I feel justified in concluding that thrombosis is not a characteristic feature of the freshly delivered uterus, that when it occurs it is a secondary process incident to the cutting off of the circulation, and that it cannot be regarded as the prime factor in the control of bleeding.

On the other hand, certain other vascular changes occur in the decidua basalis and the subjacent muscularis with much greater regularity, and when present clearly indicate the location of the placental site. These changes consist primarily in the conversion into fibrinoid tissue of the walls of both arterial and venous vessels. In this tissue the outlines of cells in various stages of preservation may be detected, while occasionally masses of similar cells lie directly beneath the endothelial lining; and exceptionally occupy the lumen as well. In some cases the lumen of the vessel is preserved, but in others it is encroached upon by the collapse of its degenerated walls with the result that hyalin structures of bizarre outline are formed, which are suggestive of somewhat similar formations observed in the ovary. In still other instances, the exterior of the vessel consists of an irregularly shaped ring of hyalin or fibrinoid material enclosing a mass of loose connective tissue, in whose center is a small and often irregularly shaped lumen, which is lined with apparently normal endothelium; while in other instances all trace of the lumen has disappeared.

These changes were noted in 27 of our 50 specimens, and while the study of a series of pregnant uteri shows that they are observed most frequently in the last months of pregnancy, they are nevertheless sometimes present during its first half. As far as I can learn these changes were first described by Patenko in 1879, but failed to create any considerable interest until recently. Since 1910, however, they have been exten-

sively studied by Frankl and Stolper, Schickele, Heckner, Hinselmann and others, but no general agreement has been reached as to their mode of production, although the prevailing opinion is that they are due to the invasion of the vessel walls by foetal elements with subsequent fibrinoid degeneration.

I am not prepared at present to express a definite opinion as to their mode of production or significance, but I expect within a reasonable time to publish a communication upon the subject, which I hope will aid in its solution. Consequently, all I can say at this time is that they were noted in more than one half of our specimens, and that in doubtful cases their presence has sometimes been the definitive factor in identifying the placental site.

I shall likewise say nothing concerning the obliteration of arteries outside of the placental site, of their regeneration in subsequent pregnancies, nor of the increase in elastic tissue which is associated with the process. These changes have been considered in detail by Balin, Pankow, Szasz-Schwarz, Goodall and others, but my opinions concerning their significance are as yet too hazy to permit me to make definite statements concerning them.

Muscular Retraction.—In considering the structure of the full-term pregnant uterus depicted in Fig. 1, attention was directed to the excessive thinness of its muscular walls, and to the fact that their fibers had lost the felt-like structure characteristic of early pregnancy and had become arranged in almost parallel strands. Coincidentally with the emptying of the uterus at the time of labor and the great increase in the thickness of its walls, the arrangement of the muscle fibers undergoes immediate change, and microscopical examination shows that the individual muscle cells have become considerably diminished in length and increased in thickness. Coincidentally with this change the muscle bundles have lost their more or less parallel arrangement and now pursue an irregular and complicated course. In many instances the fibers are markedly curved, suddenly bend at acute angles, and in general interlace in such a way as to make it impossible to describe their course.

This change, of course, is incident to the contraction and retraction of the organ, and was clearly noted in 42 of the 50 specimens.

Inflammation of the Decidua.—In the first section of the article attention was directed to the fact that in 8 instances the indication for the removal of the uterus consisted in frank intra-partum infection. In all of these cases, microscopical examination revealed the existence of acute inflammatory changes in the decidua. In every instance, the process was most intense in the lower uterine segment, thus indicating that the infection had ascended from below. In a number of instances the placental site was involved in the process, and there is every probability that a considerable number of the women would have presented severe, if not fatal, infection in the puerperium had the uterus not been removed, and thus additional evidence is afforded of the wisdom shown in adopting a radical course.

In addition to the eight cases just mentioned, definite inflammatory changes were noted in 12 other specimens. These were all derived from patients who had been examined by outside physicians before admission to the service, or in whom for one reason or another interference had been deferred until late in labor. In a number of these specimens appropriate methods of staining enabled us to demonstrate the presence of streptococci in the tissues, but in others, such bacteriological evidence could not be adduced.

The fact that inflammatory changes were present in 40 per cent of our specimens is very impressive and serves to demonstrate anew the dangers of conservative Cæsarean section when performed at any other than the optimal time—namely, at an appointed date during the last days of pregnancy or within a few hours after the onset of labor in patients who have recently been examined only by those who observe an appropriate technique. In this group of cases, at least, I feel that the disadvantages incident to permanent sterilization have been more than compensated for by the increased saving of maternal life resulting from the radical operation.

Behavior of the Cicatrix after repeated Cæsarean Section.—In our series of specimens are included 10 uteri which had already been subjected to Cæsarean section upon one or more previous occasions, and it will be interesting to study the cicatrix in connection with the frequently made statement that it always constitutes a *locus minoris resistentiæ* and thus affords justification for the dictum—"Once a Cæsarean, always a Cæsarean."

In eight of the specimens, one of which had been subjected to two and another to three previous sections, it was difficult to find the old cicatrix by examination with the naked eye, and the only indication of its existence was afforded by the presence of slight vertical depressions upon the external and internal surfaces of the uterus. In these specimens microscopic examination revealed the entire absence of scar tissue in the uterine wall and showed that the muscle fibers extended across the site of the old incision as if it had never existed.

In other words, examination showed that, following the section, the uterine wall had been restored to its integrity, and that it offered little more chance for rupture than had a previous operation not been performed. It is interesting to note that in this series of cases the convalescence from the previous operation had been uneventful and uncomplicated, at least so far as the patients operated upon by us were concerned.

In another specimen, however, totally different conditions obtained. In this a deep furrow existed upon the external surface and a corresponding furrow upon the internal surface of the contracted amputated uterus, the two being separated by a band of tissue 3 mm. thick, which contrasted markedly with the adjacent uterine walls which measured 2.5 cm. in thickness. Under the microscope it was seen that the external furrow was covered by peritoneal epithelium, while the internal furrow was lined with typical decidua. The intervening muscularis, however, showed no sign of scar tissue, and differed

from the normal only by its extreme thinness. In this instance it is apparent that the healing following the previous operation had been defective, and that during the latter part of pregnancy the portion of the uterine wall corresponding to the cicatrix must have been of extreme tenuity and offered conditions very favorable for rupture, which fortunately had not occurred. The history of this patient shows that the convalescence from the first operation had been stormy, the abdominal incision had broken down and that she had just escaped with her life.

In the last specimen, actual rupture had occurred in the eighth month of pregnancy, the foetus surrounded by the placenta and membranes having escaped into the abdominal cavity. The patient, however, exhibited no symptoms of shock, and made an uninterrupted recovery after removal of the uterus. Microscopical examination of the ruptured cicatrix showed that the placenta had been attached under it, and that the uterine walls were densely infiltrated with foetal cells. It was impossible to determine the extent to which the site of the cicatrix had been thinned out before rupture, but it is permissible to believe that the thinning had been excessive, and that the scar was still further weakened by the invasion of foetal cells and by the development of uterine sinuses, so that it had gradually yielded to the distention as term was approached. In this case, also, the recovery following the primary operation had been complicated.

The details concerning this series of cases will be published in full later, and I shall only say in this place that the evidence at our disposal indicates that the healing of Cæsarean section wounds is generally satisfactory, provided the convalescence has been normal, and ordinarily does not call for a repetition of the procedure unless definitely indicated by the existence of extreme disproportion or some other conditions. On the other hand, in patients in whom the convalescence has been abnormal, it is probable that the cicatrix will be greatly thinned out and will offer a *locus minoris resistentiæ*. In such cases, a repeated Cæsarean section may be indicated for the express purpose of avoiding a subsequent rupture. My experience, however, shows that this is not inevitable and that even should it occur, satisfactory results should follow prompt operation.

For practical purposes, therefore, I conclude that the behavior of the cicatrix can be regarded with equanimity provided the previous convalescence has been normal, but when it has been disturbed there is a reasonable probability of the occurrence of rupture, and that such patients should be kept under the closest observation during the last months of a succeeding pregnancy.

LITERATURE.

Ahlfeld: Beiträge zur Physiologie und Pathologie der Nachgeburtsperiode. Berichte und Arbeiten, 1881-1882, 40-120.

Aschoff: Beitrag zur Anatomie der Schwangerschaft. Beiträge z. path. Anat. u. allg. Path., 1899, XXV, 273-308.

Balin: Ueber das Verhalten der Blutgefäße im Uterus nach stattgehabter Geburt. Arch. f. Gyn., 1880, XV, 151-168.

Barbour: The anatomy and relation of the uterus during the third stage of labor and the first days of the puerperium. Edinburgh Med. Jour., 1884, XXX, 223-237 and 313-322.

Barbour: The third stage of labor. Edinburgh Med. Jour., 1888, XXXIV, 97-111.

Champneys: The mechanism of the third stage of labor. Trans. London Obst. Soc., 1887, XXIX, 117-146.

Curatulo: The third stage of labor. Trans. Edinb. Obst. Soc., 1894, XIX, 133-151.

Dohrn: Ein Beitrag zur mikro. Anatomie der reifen menschlichen Eihüllen. Monatschr. f. Geburtskunde, 1865, XXVI, 114-127.

Duncan: The internal surface of the uterus after delivery. Researches in Obstetrics, 1868, 186-215.

Engelmann: The mucous membrane of the uterus. Am. Jour. of Obst., 1875, VIII, 30-87.

Fehling: Die Physiologie und Pathologie des Wochenbetts. Stuttgart, 1890.

Frankl u. Stolper: Ueber den Gefäßverschluss post partum. Arch. f. Gyn., 1910, XC, 133-147.

Friedländer: Physiol. anat. Untersuchungen über den Uterus. Leipzig, 1870.

Friedländer: Ueber die Innenfläche des Uterus post partum. Arch. f. Gyn., 1878, IX, 22-23.

Gessner: Beiträge zur Pathologie der Nachgeburtsperiode. Zeitschr. f. Geb. u. Gyn., 1897, XXXVII, 17-82.

Goodall: The involution of the puerperal uterus and more particularly the involution of its circulatory system, vitreous hypertrophy and vitreous degeneration of elastic tissue. Studies from the Royal Victoria Hospital, Montreal, II, No. 3, June, 1910.

Hart: The mechanism of the separation of the placenta and membranes during labor. Proc. Royal Soc. Edinburgh, 1889, XV, 427-435.

Hart: A contribution to the pathology, symptoms and treatment of adherent placenta. Laboratory reports of the Royal College of Physicians, Edinburgh, 1890, II, 98-102.

Heckner: Beiträge zur Anatomie des Gefäßverschlusses post partum. Zeitschr. f. Geb. u. Gyn., 1912, LXXII, 281-302.

Keilmann: Uterus im Beginn der Nachgeburtsperiode. Neisser, Stereoscopischer medicinischer Atlas, 1896, VIII. Lieferung.

Kerr: The separation of the placenta, with special reference to the information derived regarding its mechanism from cases of conservative Cæsarean section. Trans. Edinburgh Obst. Soc., XXVII, 1902, 55-64.

Krönig: Beitrag zum anatomischen Verhalten der Schleimhaut der Cervix und des Uterus während der Schwangerschaft und im Frühwochenbett. Arch. f. Gyn., 1901, XLIII, 26-37.

Küstner: Die Lösung der mütterlichen Eihäute vor und bei der rechtzeitigen Geburt. Arch. f. Gyn., 1878, XIII, 422-436.

Langhans: Die Lösung der mütterlichen Eihäute. Arch. f. Gyn., 1875, XIII, 287-297.

Leopold: Studien über die Uterusschleimhaut während Menstruation, Schwangerschaft und Wochenbett. Arch. f. Gyn., 1877, XI, 443-500.

Nyhoff: Warum löst sich unter normalen Umständen die Placenta erst nach der Geburt des Kindes? Verh. d. deut. Gesellschaft f. Gyn., 1901, 576-578.

Pankow: Graviditäts—Menstruations—und Ovulationssklerose der Uterus und Ovarialgefäße. Arch. f. Gyn., LXXX, 271-282.

Patenko: Zur Lehre von der physiologischen Thrombose der Uterusgefäße während der Schwangerschaft. Arch. f. Gyn., 1879, XIV, 422-429.

Pels Leusden: Ueber die serotinalen Riesenzellen etc. Zeitschr. f. Geb. u. Gyn., 1897, XXXVI, 1-60.

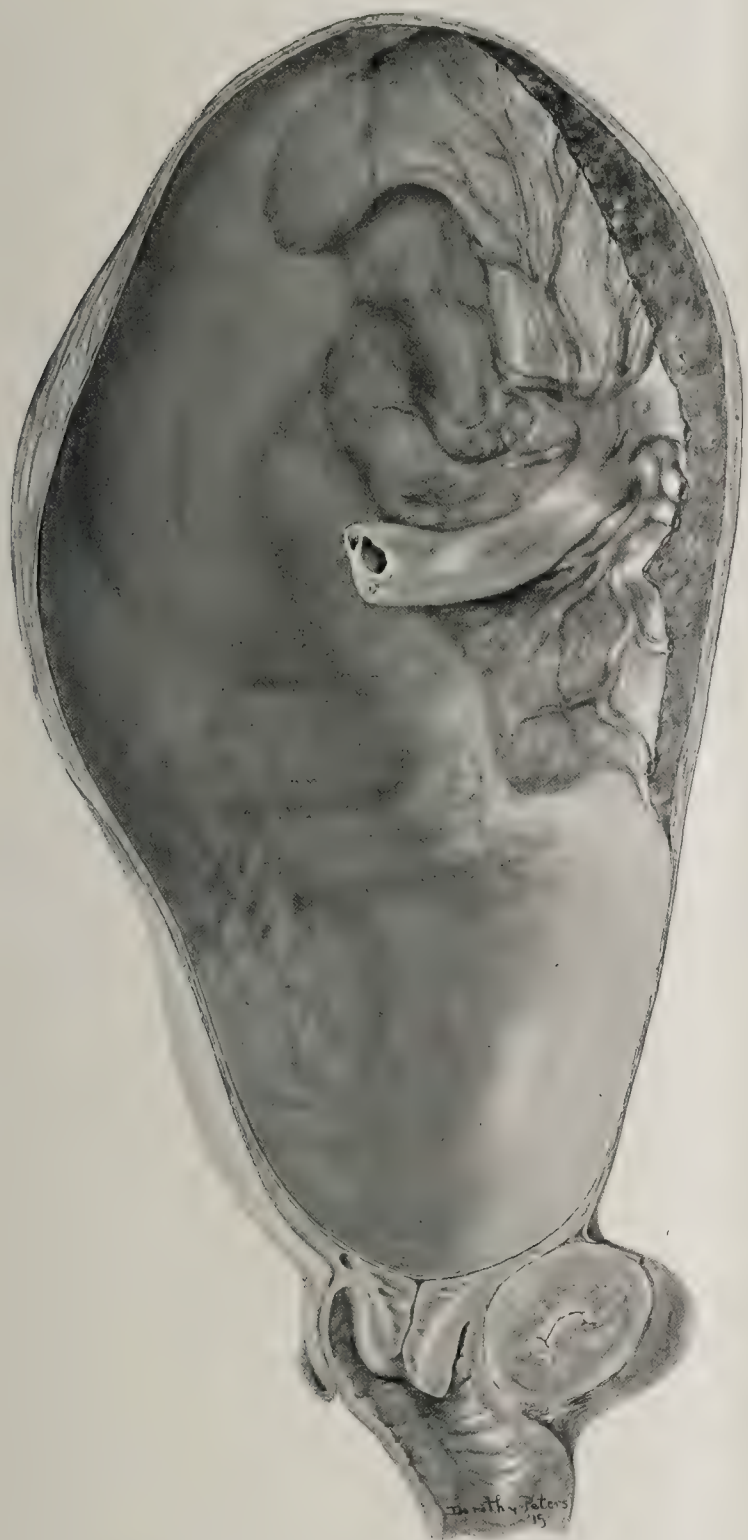


FIG. 1.—Vertical mesial section through a full-term pregnant uterus; patient dying from eclampsia before onset of labor. $\times \frac{1}{2}$.



FIG. 6.—Vertical mesial section through uterus amputated immediately post partum. $\times \frac{1}{2}$. Compare with Fig. 1, and note thick muscular walls, placenta *in situ*, obliteration of uterine cavity and festooning of fetal membranes.

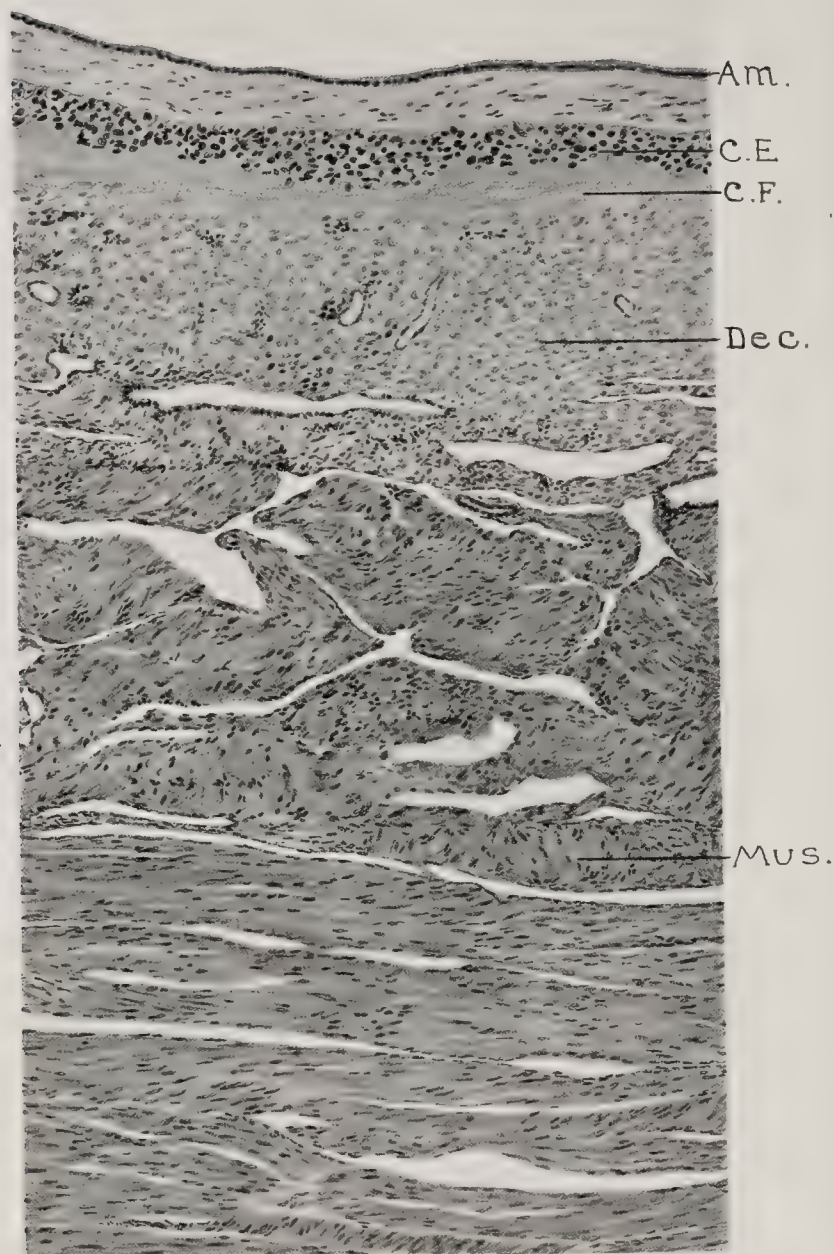


FIG. 2.—Section through uterine wall of full-term pregnant uterus outside of placental site, showing foetal membranes, decidua and muscularis. $\times 65$.

Am.—Amnion.
C. E.—Chorionic epithelium.
C. F.—Canalized fibrin.
Dec.—Fused decidua vera and capsularis.
Mus.—Muscularis.



FIG. 3.—Section through placental site before onset of labor, showing thin decidua basalis, with no spongy layer. $\times 65$.

C. V.—Chorionic villi.
Dec.—Decidua basalis.
Mus.—Muscularis showing large venous sinuses.

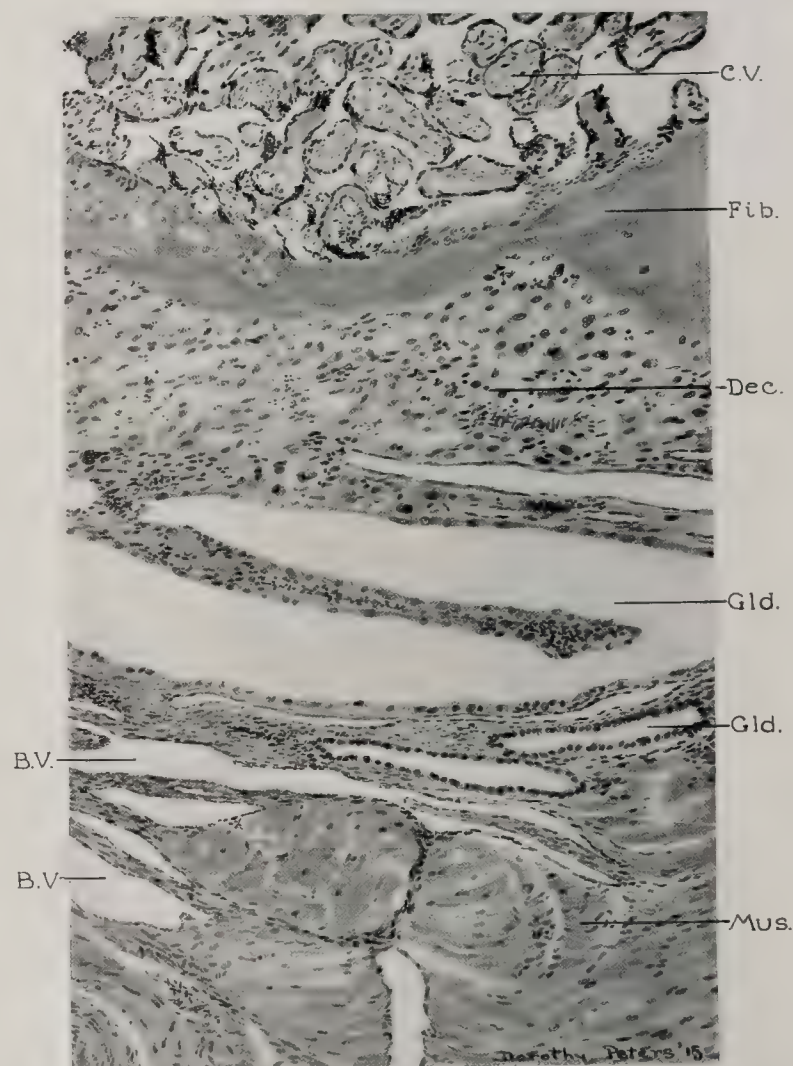


FIG. 4.—Section through placental site before onset of labor, showing thicker decidua basalis with a well-developed spongy layer. $\times 65$.

B. V.—Venous sinuses in muscularis.
C. V.—Chorionic villi.
Dec.—Compact layer of decidua.
Fib.—Fibrinoid.
Gld.—Glandular or spongy layer of decidua.
Mus.—Muscularis.

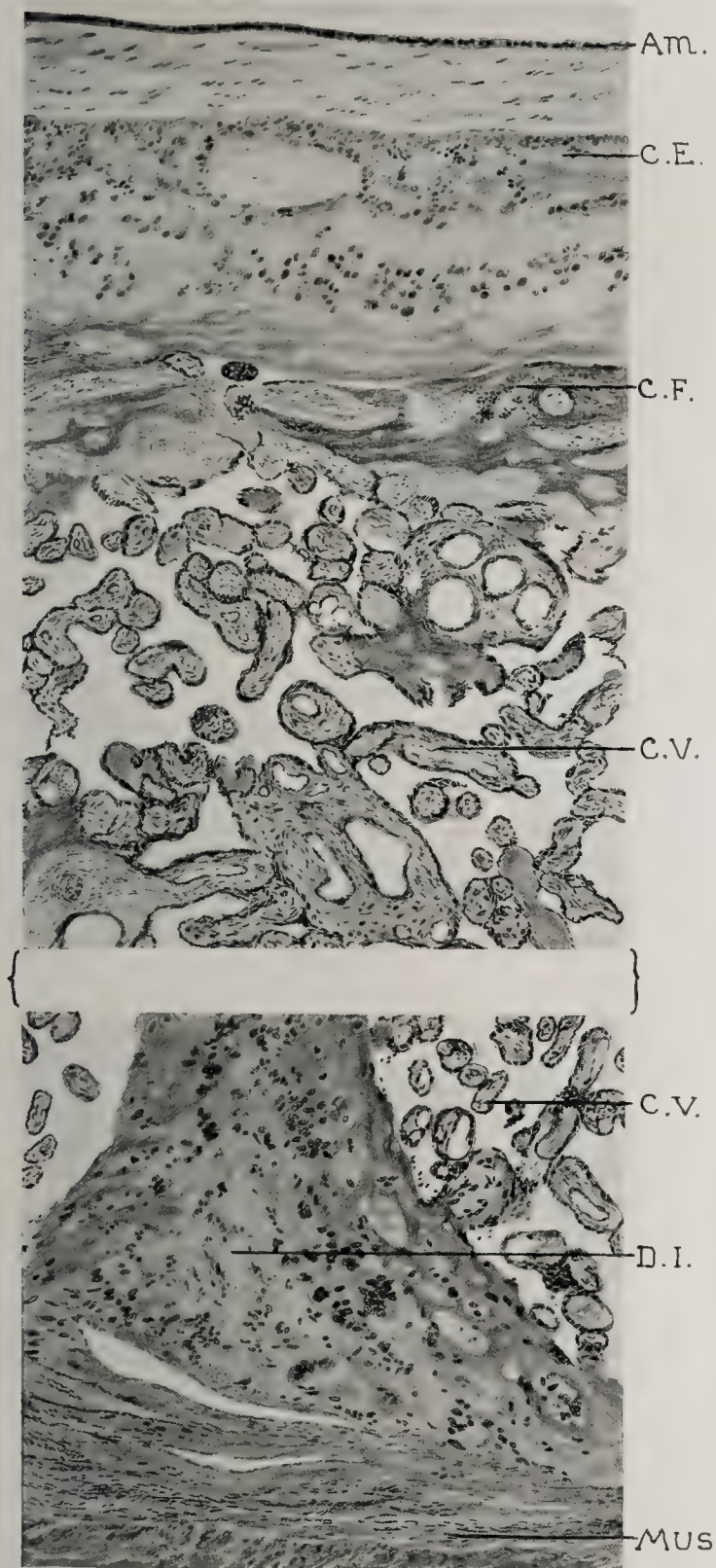


FIG. 5.—Section through placental site before onset of labor, showing above foetal aspect of placenta, below maternal aspect with thin decidua basalis and a trophoblastic septum, extending up into intervillous space. $\times 65$.
Am.—Amnion and chorionic membrane.
C. E.—Chorionic epithelium.
C. F.—Canalized fibrin.
C. V.—Chorionic villi.
D. I.—Trophoblastic septum.
Mus.—Muscularis.



FIG. 7.—Section through wall of freshly delivered uterus outside of placental site, showing festooning of membranes. $\times 24$.
Am.—Amnion.
C. E.—Chorionic epithelium.
Dec.—Decidua vera.
Mus.—Muscularis.



FIG. 8.—Portion of Fig. 7 more highly magnified. $\times 65$.
Am.—Amnion.
C. E.—Chorionic epithelium.
Gld.—Gland spaces in decidua vera.
Mus.—Muscularis.

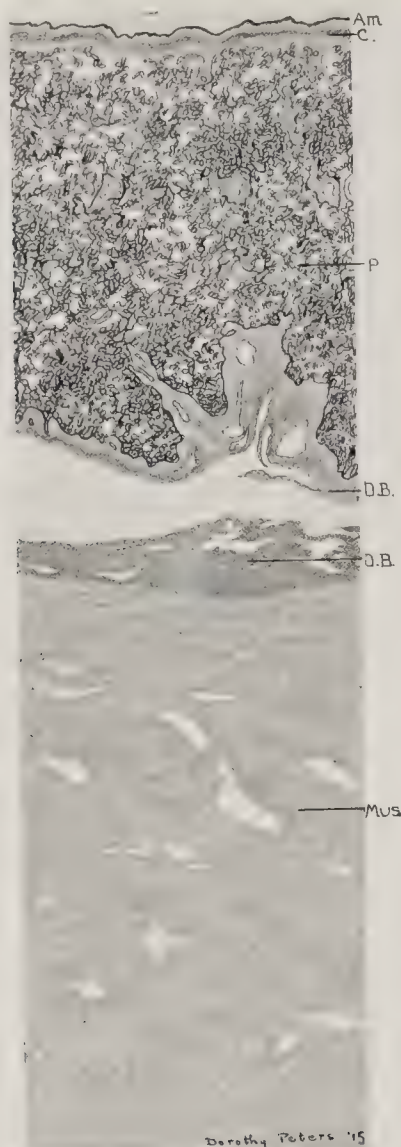


FIG. 9.—Diagram representing uterus with partially separated placenta. $\times 5$.

Am.—Amnion.
C.—Chorionic membrane.
D. B.—Decidua basalis separated into two layers with balm onlays between them.
P.—Placenta.
Mus.—Muscularis.

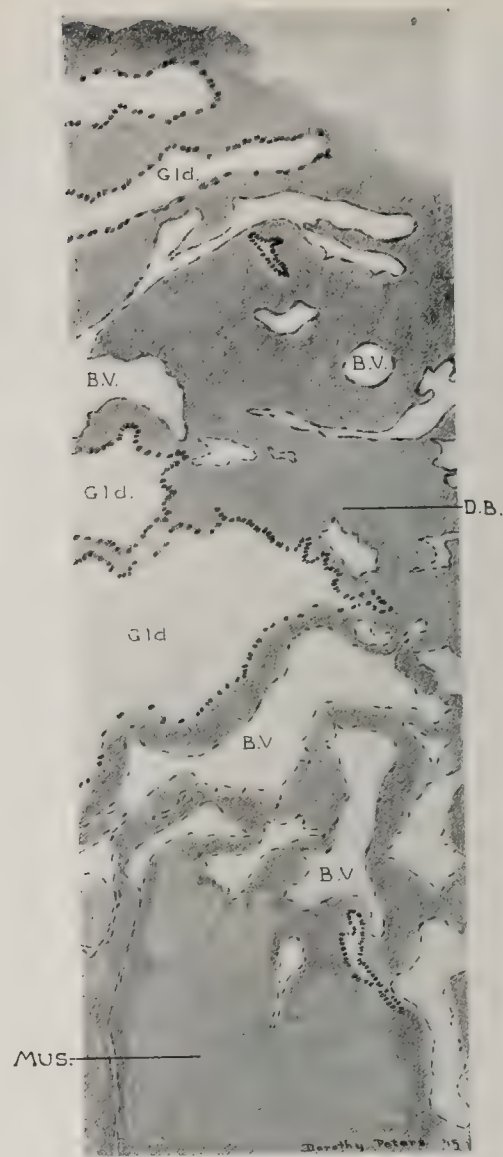


FIG. 12.—Diagram of another portion of the same placental site, represented in Fig. 11, showing retention of the greater part of the decidua basalis.

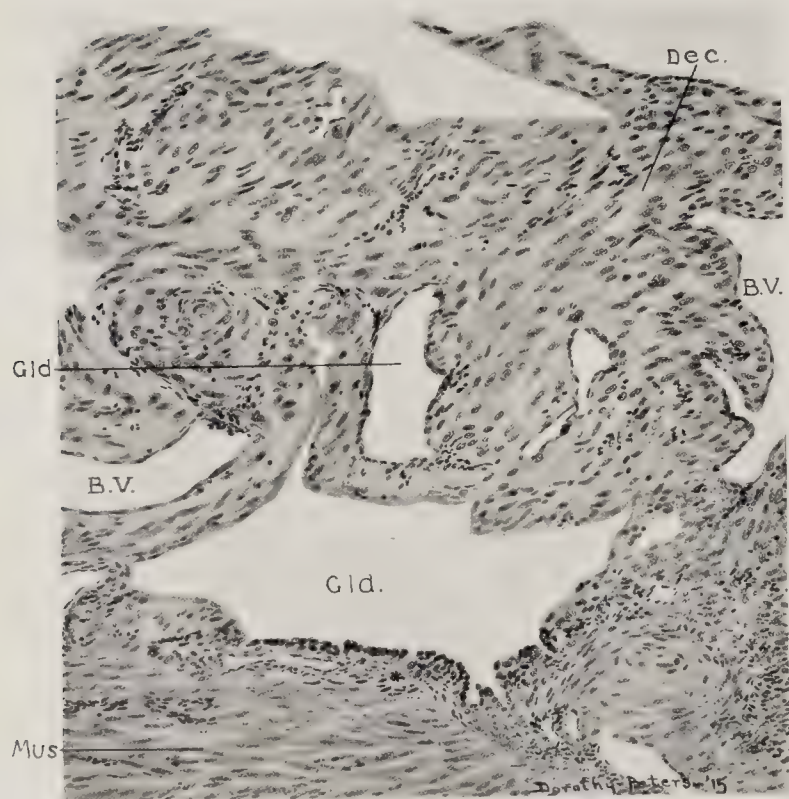


FIG. 10.—Section through freshly delivered uterus, showing that separation has occurred in the compact layer, leaving a portion of it as well as the entire spongy layer *in situ*. $\times 75$.

B. V.—Blood vessel.
Dec.—Compact layer decidua.
Gld.—Gland spaces.
Mus.—Muscularis.

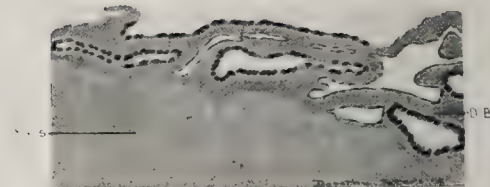


FIG. 11.—Diagram of placental site, showing retention of minimal amount of decidua basalis.

D. B.—Decidua basalis.
Mus.—Muscularis.

Pinto: Beitrag zur Kenntnis der an der Placentarstelle des schwangeren und puerperalen Uterus vorkommenden Zellelemente. *Beiträge f. Geb. u. Gyn.*, 1905, Vol. 9, 323-338.

Sänger: Neue Beiträge zur Kaiserschnittsfrage. *Arch. f. Gyn.*, 1885, XXVI, 163-233.

Schickele: Die Beziehungen der fötalen Zellwucherungen zur puerperalen Rückbildung des Uterus. *Beiträge z. Geb. u. Gyn.*, 1911, xvi, 530-560.

Schroeder & Stratz: Zur Physiologie der Austreibung und Nachgeburtsperiode. Schröder's, der Schwangere und Kreissende Uterus. 1886, 77-112.

Szasz-Schwarz: Recherches sur les altérations séniles des vaisseaux sanguins et sur le tissu élastique de l'utérus. *Revue de Gyn.*, 1903, XII, 593-626.

Winkler: Die Placentarstelle des graviden menschlichen Uterus. *Arch. f. Gyn.*, 1901, LXII, 366-414.

ADENOMYOMA OF THE RECTO-VAGINAL SEPTUM.¹

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At the meeting of the Southern Surgical and Gynecological Association in 1913² I reported two cases of this character that had recently come under my care and also gave a short survey of the existing literature.

At the meeting of the American Medical Association in 1916 I discussed the subject more fully and reported three additional cases. For an extended survey of this interesting disease the reader is referred to the paper read on that occasion.³

Adenomyoma of the recto-vaginal septum is a diffuse growth consisting of non-striated muscle and fibrous tissue with large or small areas of mucosa identical with the mucosa of the body of the uterus scattered throughout it. This mucosa swells at the menstrual period and, as there is usually no escape for the blood, the gland spaces tend to become cystic and are filled with blood; or there is hemorrhage into the matrix of the tumor.

The tumor in the beginning is very small and starts in the vaginal vault just behind the cervix; or it may be recognized as a round or irregular thickening, not over 1 cm. in diameter, behind and usually attached to the cervix. The growth gradually spreads in a diffuse and irregular manner, involves the adjacent anterior rectal wall and spreads into one or both broad ligaments, until, finally, everything in the pelvis may be firmly glued into one mass.

In my paper of 1916 I made a tentative classification. This grouping may profitably be retained until our knowledge of the subject has been augmented. The classification with the number of cases brought up to date is as follows:⁴

1. Small adenomyomas lying relatively free in the recto-vaginal septum (Cullen's Case 1, Stevens' Case 1, Stevens' Case 5, Nadal's case, Cullen's Case 6).

¹From the Gynecological Department of The Johns Hopkins Hospital and The Johns Hopkins University. Read before the American Gynecological Society, Pittsburgh, May, 1917.

²Thomas S. Cullen: Adenomyoma of the Recto-Vaginal Septum. *Trans. Southern Surg. and Gyn. Assoc.*, 1913. Adenomyoma of the Recto-Vaginal Septum. *Jour. Amer. Med. Assoc.*, March 14, 1914, p. 835.

³Thomas S. Cullen: Adenomyoma of the Recto-Vaginal Septum. *Jour. Amer. Med. Assoc.*, Aug. 5, 1916, Vol. LXVII, p. 401.

⁴For an admirable review of the foreign literature on adenomyoma of the recto-vaginal septum consult Cuthbert Lockyer in *Eden & Lockyer's New System of Gynecology*, Vol. II, p. 350. It is brim-full of interest.

2. Adenomyomas adherent to the posterior surface of the cervix and at the same time to the anterior surface of the rectum (Lockyer's Case 2, Cullen's Case 3, Stevens' Cases 2, 3, 4 and 6, Jessup's Cases 1 and 2).

3. Adenomyomas gluing the cervix and rectum together and spreading out into one or both broad ligaments (Cullen's Case 4, Cullen's and Richardson's Case 5, Kellogg's case,⁵ Cullen's Cases 7, 8 and 9).

4. Adenomyomas involving the posterior surface of the cervix, the rectum and broad ligaments, and forming a dense pelvic mass that cannot be liberated (Cullen's Case 2).

Of course, one group merges imperceptibly into another, and a case which to-day belongs to Group 1 may in a few years belong to Group 2 or to Group 3.

Case 6 is one of the earliest adenomyomas on record and was diagnosed clinically. Case 7 is particularly interesting. The adenomyomatous growth was evidently a very active one, so active that it welled out into the vagina forming adenomyomatous polypi which projected into the vagina, and at some points areas of uterine mucosa lay in direct contact with the cavity of the vagina. It was from the histological examination of one of the vaginal polypi that the exact diagnosis was made. In this case, as will be noted from Fig. 3, both ureters were encircled and constricted by the adenomyomatous growth in the broad ligaments, so much so that above the point of involvement the ureters were greatly dilated, each being over 1 cm. in diameter. At the menstrual period with the swelling up of the uterine mucosa in the adenomyomatous areas the ureteral constriction was increased and the patient experienced pain in both renal regions.

In Case 8 the growth was very extensive, having involved the anterior and lateral rectal walls over an area about 9 cm. in length. The growth seemed to have developed within the space of two years. In this case also uterine mucosa projected directly into the vagina.

In Case 9 the growth has not yet been removed. The symptoms present were in large measure due to tuberculous pus tubes.

As can readily be inferred the symptoms will in large measure depend on the manner in which the growth extends. When small it occasions little trouble. Extension to the rectum may or may not be followed by pain. Implication of

⁵Kellogg: *Boston Med. and Surg. Jour.*, Jan. 4, 1917, p. 22.

the pelvic nerves in the diffuse growth may cause much neuralgic pain and encircling of the ureters by the growth may bring about unilateral or bilateral hydroureter with renal pressure symptoms at the periods.

Menstruation in some cases occasions much pain. If the mucosa of the growth has projected into the vagina, there will be an escape of menstrual blood from the posterior vaginal wall at the catamenial period, as was noted in Case 8 in which the patient menstruated, although her uterus had been removed two years before.

In those cases in which the glands of the adenomyoma extend through to the rectal mucosa there will naturally be some escape of menstrual blood from the bowel at the period—as in Case 8.

In all of the previous cases the tumor occurred during menstrual life. The four cases here recorded offer no exception to the rule. The patients were 28, 37, 27 and 43 years of age.

We know nothing as to the origin of these tumors, but it is certain that their glandular elements are identical with those of the mucosa of the body of the uterus. A careful survey of the wealth of embryological material in Professor Mall's laboratory may give us some clue as to the starting-point of these growths.

TREATMENT.

We have had no occasion to change the line of treatment suggested in the paper of 1916.

Some might argue that simple removal of the appendages would cause atrophy of the uterine mucosa contained in the adenomyomas of the recto-vaginal septum. My Case 2 is a sufficient answer. Although a supravaginal hysterectomy had been performed two years before for a myomatous uterus, the pelvic condition had grown steadily worse.

1. Where small discrete nodules exist in the posterior vaginal vault, these may be readily removed through a vaginal incision, as was so successfully done by Stevens.

2. Where the growth occupies the posterior surface of the cervix and extends laterally, the ureters should be dissected out carefully and a complete abdominal hysterectomy be performed.

3. If the growth be firmly adherent to the rectum, a wedge of the rectum should be removed, together with the uterus. It has been found best, after freeing the uterus on all sides, to open up the vagina anteriorly and laterally. The uterus and the rectum can then be lifted farther out of the pelvis, thus facilitating the removal of the necessary wedge of the anterior rectal wall. The uterus can be used as a handle, and the necessary rectal tissue and the uterus removed as one piece.

4. Where the lumen of the bowel is greatly narrowed, a complete segment of the rectum should be removed together with the uterus, and an anastomosis made.

5. In desperate cases, where everything in the pelvis is glued together, as in my Case 2, an ideal procedure is out of the question. The patient will not stand a long operation and, if she could, a satisfactory result could not be obtained.

In such a case it would be better to cut across the sigmoid, invert the lower end, close it, and bring the upper end out through the abdominal wall of the left iliac fossa, making a permanent colostomy. When the patient has to some extent regained her strength, the uterus, the lower portion of the rectum and the broad ligament tissue can be shelled out as one piece.

These growths, while histologically not malignant, remind one of glue. Unless they are completely removed, further trouble is liable to occur.

Case 6 was simple and the woman made an excellent recovery.

In Case 7 the patient was too weak to allow us to resect the bowel and a portion of the growth still remains in the anterior recto-vaginal wall. Radium has been used, but the growth in the rectal wall is becoming thicker and sooner or later, I believe, it will be necessary to remove the portion of the rectum that is involved.

In Case 8 the operation had progressed so far that we were forced to resect the rectal growth. Had it not been for the wonderful assistance rendered by those helping at the operation, supplemented by the excellent post-operative nursing, this patient would certainly have succumbed. As it was, her life time and again was hanging in the balance. She will recover.

In Case 9 the adenomyoma still remains.

The occurrence of nine cases in the practice of one surgeon needs little comment. The disease is by no means rare. In the early stages it has naturally been overlooked. In the late stages it has been taken for an extensive and intractable inflammation in the vaginal vault or for a malignant growth involving the vagina and rectum.

CASE 6.—A very early adenomyoma of the recto-vaginal septum associated with a polypoid condition of the endometrium which showed marked hyperplasia—early adenomyoma of the uterine wall.

C. H. I., No. 15496.—Mrs. J. S., aged 43, was seen in consultation with Dr. Wilbur Pearce, on Sept. 19, 1916. This patient began menstruating at fifteen. The periods were always regular until her child was born 18 years ago. Since then she has suffered with pain in the right lower abdomen at the time of menstruation. The periods have been very irregular and the amount of pain has progressively increased, and has been especially marked during the last two or three years. The periods last from 5 to 15 days. There is often only an interval of from a few days to a week between periods. The pain has often been so severe that the patient has had to remain in bed for several days each month. She has had slight leucorrhœa.

On pelvic examination I found the uterus about half as large again as normal and just posterior to the cervix was a little puckered and thickened area apparently not over 1 cm. in diameter. I immediately suspected adenomyoma of the recto-vaginal septum.

Operation September 20.—We dilated and curetted, removing a moderate amount of tissue which in the frozen section showed hyperplasia. On account of the persistent bleeding and the fact that adenomyoma of the recto-vaginal septum existed, I decided to remove the uterus by the abdominal route. After dissecting free both ureters I did a complete hysterectomy, removing with the uterus the puckered area of peritoneum lying just posterior to the cervix (Fig. 1). This area of puckering was star-shaped.

A drain was laid from the pelvis into the vagina. The patient made an uninterrupted recovery and was allowed out of bed on the 15th day.

Gyn.-Path. No. 22483.—The uterus is 10 cm. long, 5 cm. broad and 4 cm. in its antero-posterior diameters. On the posterior surface of the uterus just on a level with the lower edge of the cervix is a puckered area 1 cm. in diameter. This at the time of operation was clearly visible and rather hard. The underlying tissue is slightly indurated and strongly suggests adenomyoma. The uterus itself apart from this is perfectly smooth. The appendages were not removed.

As mentioned above, just prior to the hysterectomy a dilatation and curettage had been done and the tissue, which was examined immediately, showed hyperplasia. On opening the uterus we found that, notwithstanding the curetting, the cavity was two-thirds filled with a rather polypoid, somewhat fibrous growth, which at the fundus reached 1.5 cm. in thickness.

Sections from the body of the uterus show that the uterine mucosa has an intact surface epithelium. The glands are large or small and have an epithelium that is thicker than usual. There is a definite tendency for the mucosa to extend into the underlying muscle, in other words, there is without doubt a beginning adenomyoma. The polypoid thickening consists of uterine mucosa. The glands here are large, tortuous and lined with thickened epithelium; the stroma is exceedingly cellular. One is able here and there to make out nuclear figures in the stroma. The picture is that of a typical hyperplasia of the endometrium. There is no evidence whatever of malignancy.

In this uterus, then, we have a definite hyperplasia of the endometrium with an unusually abundant polypoid formation of the mucosa. The uterine glands are also extending into the underlying muscle, producing an early adenomyoma.

The puckered area on the posterior surface of the uterus just at its junction with the cervix (Fig. 1)—the area that was recognized clinically—consists of myomatous tissue and glands (Fig. 2). These glands are tortuous, are lined with one or more layers of cylindrical epithelium and are in many places separated from the surrounding muscle by a stroma resembling in every particular that of the uterine mucosa. Some of the glands are dilated and we have a few miniature uterine cavities. All of the cavities and some of the glands show fresh hemorrhage. The picture present is that of a typical adenomyoma of the recto-vaginal septum. This is one of the few cases that we have been able to diagnose clinically before operation.

July 12, 1917.—About four weeks after returning home the patient lost bright red blood from the bowel. Near Christmas (1916) there was again bleeding, which continued for several days, the blood being bright red. In March, 1917 there was bleeding from the bowel for four days, and in the middle of April for four days. Bleeding started one week ago and has just stopped. She gives a history of having had bleeding from the bowel four years ago lasting for six weeks.

On proctoscopic examination the rectal mucosa looks perfectly normal and is nowhere thickened. The bleeding evidently comes from higher up in the bowel.

CASE 7.—Advanced adenomyoma of the recto-vaginal septum constricting both ureters and causing double hydronephrosis. Extension of the adenomyoma into the vagina forming adenomyomatous polypi which hung down in the vaginal vault behind the cervix.

For this most instructive case I am indebted to Dr. Myer Solis-Cohen of Philadelphia, her physician, and to Dr. Alfred Heineberg, the surgeon who saw her on numerous occasions and who removed several of the vaginal polypi. So far as I can learn, this case is unique.

Dr. Alfred Heineberg, in reporting this case in the *American Journal of Obstetrics* (March, 1917, p. 385), says: "The patient Miss —, aged 27, was referred to me by Dr. Myer Solis-Cohen of

Philadelphia, on February 11, 1916, with the following history: About two years before she had been seized during her menstrual period with sudden severe pain in the rectum which radiated down the left thigh to the knee. This recurred with each succeeding period and was associated with menorrhagia until she was subjected to operation on Aug. 13, 1914. At this operation the uterus was dilated and curetted, and an abdominal incision was made. In the left ovary was found a cyst about the size of an orange, filled with old blood. There was a small quantity of similar bloody fluid free in the peritoneal cavity.

"Adhesions of the intestine to the pelvic structures required breaking up, and the left tube and ovary and appendix were removed. A rubber drainage-tube was inserted in the lower angle of the incision.

"For three months after operation she experienced slight relief in the symptoms, but by February, 1916, she was suffering severely and was again examined and two small polypi attached to the posterior vaginal wall were found. These were removed under gas anæsthesia but their removal afforded no relief.

"On July 23, 1915, several small polypi were again found in the same location. In addition to the menorrhagia she had noticed slight vaginal bleeding between periods. She refused further examination or operative treatment until Feb. 11, 1916, when I was requested to see her. On close questioning I learned that the rectal pain began on the fourth day of each menstrual period and persisted for several days after the cessation of the flow which was profuse and of 12 or 13 days' duration. On vaginal examination several small polypi were discovered attached to the posterior vaginal wall about 1 cm. below the vaginal portion of the cervix which was in no way connected with the tumor. They were soft like an ordinary mucous polyp of the uterus but somewhat more friable and bled from the slightest traumatism of the examination. The area of the vaginal wall to which the polypi were attached and the subjacent connective tissue were found indurated and thickened, imparting to the finger the sensation of a cellulitis of long standing. This indurated area was flattened and extended somewhat to each side into the base of the broad ligament. It could be more thoroughly outlined by a finger in the rectum and at the same time the mobility of the rectal mucous membrane over it was distinctly determined. The friability of the polypi, their tendency to bleed and their recurrence after the previous removal caused me to regard them as malignant. I was at a loss at first to account for either a benign or malignant polypoid growth in the posterior vaginal wall, because such growths are, as a rule, of glandular origin and the vaginal mucosa is usually devoid of glands.

"In order to avoid an unnecessarily extensive operation with the certain loss of the uterus in a young unmarried woman, I decided first to remove the polypi and subject them to histological study. If they proved to be malignant a subsequent abdominal operation would be imperative."

Dr. Heineberg removed these polypi under gas anæsthesia. They were pinkish in color. They were removed with the curette and the bleeding surface was cauterized with the actual cautery and the vagina tamponed. Heineberg says: "In spite of the precautions taken to produce hemostasis the patient suffered profuse bleeding from the vagina on the fifth and seventh days after the operation. The bleeding was again controlled by tampons. The patient left the hospital on the fourteenth day."

Dr. Heineberg did not examine the patient again until August 30, 1916. Dr. Myer Solis-Cohen had reported from time to time that there was no apparent change in her condition. At the examination on August 30, he found that the indurated mass in the recto-vaginal septum had increased somewhat in size since the previous operation and that it seemed to be attached to the supra-vaginal portion of the cervix. He discovered another small polyp about half the size of a pea at the site of the previous ones. This

he removed with the finger without difficulty. He sent this polyp to me for histological examination.

My report was as follows:

"On histological examination some of the polypoid projections are found to be covered over by many layers of squamous epithelium similar to that noted in the vaginal vault. The surface of others consists of typical granulation tissue. In other words, there has been an ulceration of some of the polypi. The stroma immediately underlying the surface consists of rather dense connective tissue. Deeper down are large numbers of glands, some very large and surrounded by a characteristic stroma, others small and lying in direct contact with the surrounding connective tissue. Some of the larger glands are filled with blood. The glands are of the type found in the body of the uterus and the general gland picture is that we often note where glandular hyperplasia exists. At a few points the stroma cells are swollen and remind one considerably of the interlacing of large cells noted in an early sarcoma. I do not, however, think that this feature is of the slightest significance."

A few days later Dr. Heineberg sent me some more tissue from the vaginal vault. My findings were as follows:

"The polypoid mass that you sent me on September 20, 1916, has been marked Gyn.-Path. No. 22482. On the surface of this polyp I failed to find any evidence of vaginal mucosa. There is, however, a granulating surface and opening on the surface are typical uterine glands. This section brings out another interesting feature. Here and there throughout the stroma are yellowish-brown pigmented areas. At such points the stroma cells have taken up blood pigment, clearly showing that there have been old hemorrhages."

It was clearly evident that we were dealing with an adenomyoma of the recto-vaginal septum and I advised complete hysterectomy with, if possible, removal of the portion of the anterior rectal wall that had become involved in the growth.

Gyn. No. 22645.—The patient on admission to The Johns Hopkins Hospital, on November 16, 1916, was rather frail and somewhat anæmic. Her temperature was 99.2° F. and her pulse 88. On physical examination, however, it reached 120.

The patient said that she first developed symptoms of the present trouble in December, 1913, when she had pain during the last three days of the menstrual period. The discomfort was mild at first, but has gradually increased in severity. The pain is located in the rectum. At present it is very severe and she feels "as if the bowels must move." She has had no pain between periods and defecation does not cause discomfort, but digital examination of the rectum and enemata cause excruciating pain. There has been no bleeding from the bowel. The patient has slight dysuria and frequency of urination. During the last three days of the period there has also been a very marked desire to urinate frequently without the ability to do so.

Recently she has complained of severe pain in both renal regions during the period. A glance at Fig. 3 will clearly explain the cause.

The outlet was intact. The cervix rather fixed, firm and about normal in size. The body of the uterus was slightly enlarged, in good position, but its mobility was restricted.

Projecting from the vaginal vault posterior to the cervix were several polypi. (Fig. 4.) These were blunt or rather pointed. Some of them were dark blue or bluish black in color. The vaginal vault between the cervix and rectum was hard and thickened over an area about 3 cm. in breadth. On rectal examination the rectal mucosa was found intact, but the anterior rectal wall was hard and infiltrated and the cervix and anterior wall of the rectum would move as one piece.

Operation November 18, 1916.—When the abdomen was opened, there were found numerous omental adhesions to the anterior abdominal wall and also to the pelvic structures. These were

released. It was also necessary to free several loops of small bowel that had become adherent in the pelvis.

The left round ligament was ligated and cut and the broad ligament opened. This enabled me to draw the uterus up a little. The right round ligament was now severed and the right broad ligament opened. On carrying the dissection down, the right ureter was found to be over 1 cm. in diameter. (Fig. 3.) The diffuse growth which involved the posterior wall of the cervix and the anterior rectal wall had extended out into the broad ligament and the ureter ran through this. The right ureter was gradually tunneled out of this tissue by stretching the tissue with a pair of long Kelly forceps. The uterine artery was doubly ligated and cut and the ureter exposed. Where it passed through the adenomyomatous tissue it was markedly constricted being not over one-half its normal size. Near the bladder, where it was free from compression, it was also somewhat dilated, being about 6 mm. in diameter.

The bladder was now separated from the cervix and pushed down.

The left ureter was much dilated being nearly as large as the right. It likewise was markedly constricted where it passed through the broad ligament. Here it lay completely encircled in adenomyomatous tissue. Near the bladder its calibre was slightly larger than normal. After doubly ligating and severing the left uterine artery and controlling all large vaginal veins, we freed the vagina for a distance of at least 3 cm. The uterus together with a cuff of vaginal mucosa nearly 3 cm. broad was removed. (Fig. 4.) We had hoped to remove the hardened area of the anterior rectal wall with the uterus but the patient's pulse was very weak, so we cut the cervix away from the rectum removing only the uterus with a large vaginal cuff and the right tube which was enveloped in adhesions. The right ovary was not removed.

An area of growth at least 3 x 2 cm. was left in the anterior rectal wall. After checking all oozing and whipping over the cut margins of the vagina, each ureter was lifted well up to the side of the pelvis so that it could not come in contact with the rectal growth. The broad ligaments were then closed and the raw surface of the rectum covered over as well as possible. Two drains were laid in the pelvis, their lower ends being brought out through the vagina.

The patient was discharged on Dec. 13, 1916, and at that time was entirely free from her previous discomfort. Hoping to diminish the size of the rectal growth or to at least check its progress I conferred with Dr. Curtis F. Burnam as to the use of radium. He has given her three applications and thinks that the rectal thickening is diminishing.

June 30, 1917.—I saw Miss Q., with Dr. Myer Solis-Cohen and Dr. Burnam. She looks remarkably well but when tired often has projectile vomiting. She also has rectal pain for five or six days at what should be the normal time for the period.

On vaginal examination the vault is found firmly closed, and but little thickening can be detected, but on rectal examination it is clearly evident that the growth in the anterior rectal wall has increased in thickness. One gets the impression that it is at least 1.5 cm. thick. Rectal examination occasions no bleeding and causes little pain.

July 24, 1917.—The patient says that she has had no pain in the kidney regions since operation.

Gyn.-Path. No. 23116.—The uterus is 10 cm. long, 5 cm. broad and 4 cm. in its antero-posterior diameters. Both anteriorly and posteriorly it is covered by adhesions. In the anterior surface of the fundus are two small myomata, the larger of the two being 9 mm. in diameter.

The cervix looks normal (Fig. 4). It is surrounded by a cuff of vaginal mucosa varying from one to two or more centimeters in breadth. The vaginal mucosa anterior to the cervix is unaltered, but behind the cervix polypi are seen springing from the mucosa.

These polypi are bluish-black in color, blunt or pointed, and project from 5 to 10 mm. from the surface of the mucosa.

When the uterus is cut lengthwise (Fig. 5) it is noted that the uterine walls as a whole present the usual appearance and that the mucosa of both cervix and body seems to be unaltered.

Commencing about 8 mm. behind the cervical canal and intimately blended with the cervical wall is a diffuse, striated growth, which reaches upward as far as the level of the internal os. It has dark patches and translucent areas scattered throughout it. The largest of the dark areas is 7 mm. long. The posterior surface of this growth was intimately blended with the rectum. It is from the lower surface of this growth that the polypi grew. In other words the polypi are portions of the growth which have projected into the vagina.

Histological Examination.—The character of the growth is particularly well shown in Fig. 6. The anterior wall of the cervix is normal and the mucosa lining the cervical canal presents the usual appearance. The greater part of the posterior wall of the cervix is markedly altered. It has a somewhat striated structure and scattered everywhere throughout it are quantities of typical uterine mucosa. This is recognized as islands of mucosa, as broad branching rivers of mucosa, or as miniature uterine cavities, as is well shown in Fig. 6 at *c*. The nearer one approaches the rectal attachment the more abundant is the uterine mucosa.

Not only is the posterior wall of the cervix involved in the growth but it has also extended to the vaginal wall. Islands of typical uterine mucosa are lying directly beneath the vaginal mucosa, or have broken through as shown in Fig. 6 at *b*, and in Fig. 11 between *c* and *c'*.

In Fig. 7 the character of the mucosa is clearly shown. The glands are tubular and are separated from one another and from the surrounding muscular and fibrous tissue by a definite stroma identical with that found in the mucosa lining the uterine cavity. In Fig. 8 we have a good example of a miniature uterine cavity, an area of typical uterine mucosa projecting into it. In Fig. 9 is a large mass of uterine mucosa projecting into and nearly filling a cervical gland. The cervical mucosa looks perfectly normal and is taking no part whatever in the growth.

The polypi projecting into the posterior vaginal wall are part and parcel of the adenomyomatous growth. The stroma of the polypi consists in large measure of fibrous tissue, and scattered throughout the stroma are glands of the type found normally in the mucosa from the body of the uterus (Fig. 10, Fig. 11, and Fig. 12). Some of the polypi are covered over by normal vaginal mucosa, but in others the growth has broken through the vaginal mucosa and polypi indistinguishable from those found in the uterine cavity are projecting directly from the vaginal vault (Fig. 11*a*).

The histological picture clearly shows that we have here an adenomyoma occupying the posterior wall of the cervix. This has extended by continuity to the rectum, and has infiltrated the posterior vaginal wall. The growth has been of such an exuberant character that it welled into the posterior vaginal vault, forming polypi, and in some places the growth has literally burst into the vagina, uterine mucosa projecting into and lining the vaginal vault.

CASE 8.—Myomectomy, without interruption of pregnancy, in 1907. Supravaginal hysterectomy for myoma, in 1915. Removal of the cervix and several inches of rectum for adenomyoma of the recto-vaginal septum, in 1917.

Mrs. L. D. K., aged 27, was referred to me by Dr. A. S. Mason, of Hagerstown, on August 5, 1907. She had had no children and no miscarriages. Her menses had begun at 12, had been regular and the flow moderate, the last period having occurred on May 28, 1907.

She was complaining of pain in the right ovarian region and two weeks before had noticed a lump there. During the last six

weeks she had been complaining of morning sickness and the breasts had been slightly enlarged.

On abdominal examination I found a movable, slightly nodular mass, about 8 cm. in diameter, midway between the anterior superior spine and the umbilicus on the right. On vaginal examination the mucosa was found to be rather soft, the cervix was softened and the body of the uterus somewhat enlarged.

Operation.—We made a right rectus incision and found a sub-peritoneal pedunculated myoma, 8 cm. in diameter. This was attached by a pedicle 3 cm. broad and 0.5 cm. thick. The myoma was removed and the pedicle whipped over with catgut. The appendix was slightly enlarged but was not disturbed, as we were a little afraid of infection in face of the vascular myoma and the existence of pregnancy.

The patient went on to term and was delivered of a normal child who at the present time is perfectly well.

Two years ago (June, 1915) Dr. A. L. Stavelly, of Washington, saw this patient and found it necessary to do a supravaginal hysterectomy for myoma. He found numerous adhesions, removed both tubes, the left ovary and the appendix. The patient was much improved. Her general health was better, she had no headaches and the bearing-down pains from which she had suffered were completely relieved for two months. She, however, had a good deal of constipation.

Menstruation following Hysterectomy.—Following operation although the uterus had been removed, the patient continued to have her menstrual periods. They came on regularly every month. They were slight in amount except on one occasion, when in January, 1917, although they were scanty, they continued for 28 days. The patient said that there had been a change in color of the menstrual flow for the last eight months. Before the hysterectomy and for about a year following the operation the menstrual blood had always been bright red, but during the last eight months it had been dark red and contained mucus. For the past year at times there had been intermenstrual bleeding varying in amount and frequency. This intermenstrual bleeding was sometimes noticed from the vagina, sometimes from the rectum and at times there had been more bleeding from the rectum than from the vagina. For the past year at least the patient had menstruated more frequently from the rectum than from the vagina. The dysmenorrhœa from which she had been suffering for some time was relieved for a short time after the operation but later had become increasingly severe.

The patient had been suffering from a marked constipation, intermittent in character. During the last few days of menstruation she has had severe constipation with aching pain on defecation. The constipation would last for two weeks at a time and then disappear as the menstrual period approached. During the period of constipation there would be dark blood in the stools. As soon as the period ceased, the constipation would develop again and continue for at least two weeks.

Dr. Stavelly in a recent examination found a good deal of thickening in the vaginal vault behind the cervix and came to the conclusion that the patient was suffering from an adenomyoma of the recto-vaginal septum.

Gyn. No. 23289.—This patient was admitted to The Johns Hopkins Hospital on May 24, 1917. At the present time she is well nourished and looks perfectly well. She, however, complains of severe rectal and abdominal pain at the menstrual period.

Operation May 26, 1917.—I made a median abdominal incision and found the sigmoid flexure adherent to the posterior surface of the cervix. The adhesions were gradually loosened. We dissected out the left ureter in its pelvic portion and then the right ureter, after which the bladder was pushed down from the cervix. After large vaginal veins had been tied, the vagina was freed for a distance of several centimeters. We then opened up the anterior vaginal wall and gradually severed the posterior wall

of the vagina. As we were freeing the posterior vaginal wall there was an escape of an inky black fluid from the vagina just behind the cervix. Having completely separated the cervix with the vaginal cuff from the remaining portion of the vagina, we still found the cervix firmly glued to the rectum over a wide area. The patient's condition at that time was fairly good and I thought it might be possible to remove the anterior rectal wall without sacrificing the lateral and posterior walls, which would have simplified the operation materially. When we had done this, however, we found that there remained only a ribbon of the posterior rectal wall about 1.5 cm. broad; consequently we had to do a complete resection, removing about 12 cm. of the rectum. There was an escape of a good deal of liquid fecal matter. This, of course, could have been avoided had we at first attempted a complete resection of the segment of the bowel. The patient's condition now was precarious and it looked as if she would die on the table. We hurriedly stitched a rubber tube, about 1.5 cm. in diameter, into the upper cut end of the sigmoid and drew it down so that this part of the bowel passed into the lower segment. Two continuous rows of sutures completed the end-to-end anastomosis. A drain was laid in each broad ligament and brought out through the vagina. We also drained through the lower end of the abdominal incision. When the patient left the table she was practically pulseless. The operation in its entirety occupied nearly three hours.

July 12, 1917.—The patient had a stormy time for fully two and a half weeks following operation. For the first nine days all the urine was passed through the urethra, but on the 10th day it commenced to come through the vagina. The rectal tube came out on the seventh day and since then the major portion of the feces has escaped through the vagina. On the eighth day the patient developed a diarrhoea and had many stools each day. These stools were gradually checked. Since the fifteenth day there has been a gradual improvement and at the present time, July 12, the patient is able to be out of bed for several hours each day.

There is a hole 1.5 cm. in diameter in the anterior rectal wall at the site of the anastomosis.

October 16, 1917.—Patient's condition fair.

Gyn.-Path. No. 23074.—The specimen consists of the cervix and a segment of the rectum several inches in length. (Fig. 13.)

The vaginal portion of the cervix is 5 cm. broad, 3 cm. in its antero-posterior diameters; it projects for 1 cm. into the vagina. The cervical opening is slit-like and 1 cm. broad.

The cervix looks normal. It is surrounded by a vaginal cuff, averaging 1 cm. in breadth. Posteriorly where the cervix joins the vagina is a dark transverse slit 7 mm. long. It was from this point that the inky black blood escaped during the operation. At this point the growth has apparently broken through the vaginal mucosa.

It will be remembered that the body of the uterus was removed by Dr. A. L. Stavely two years ago on account of a myoma. The cervix is 5 cm. in length. On its right side near the peritoneal reflection is a bean-shaped myoma, 1.5 x 0.9 cm.

Occupying the posterior wall of the cervix and spreading out into the anterior and lateral rectal walls is a diffuse and very hard growth.

The portion of the rectal wall removed is 12.5 cm. long. Its anterior and lateral walls vary from 1 to 2 cm. in thickness, and are board-like, owing to the diffuse growth which occupies the cervix and adjacent rectal wall.

The anterior rectal wall is thickened over an area about 9 cm. in length, the greatest thickening being near the cervical attachment.

The mucosa of the anterior rectal wall is in some places stretched out and flattened over the growth. In other places it is

gathered up into small polypi. The power of contractility of the anterior rectal wall has been reduced to the minimum.

At a point directly behind the cervix there is a dark hemorrhagic area 1 cm. in diameter in the rectal mucosa. Whether this has been caused during the operation or has been due to an extension of the growth through into the lumen of the bowel is uncertain. The mucosa from the posterior rectal wall looks normal.

On making a sagittal section through the specimen (Fig. 13) the anterior lip of the cervix is found to be little altered, save for one hemorrhagic spot, 2 x 2 mm., situated well above the vaginal attachment. The cervical mucosa looks normal except for a very small polyp projecting into the cervical canal.

The posterior wall of the cervix is markedly altered. It is occupied by a diffuse finely striated growth which extends almost from the cervical canal back to the thickened growth in the anterior rectal wall, with which it is continuous.

In the posterior wall of the cervix and separated from the outer surface of the cervix by a distance of 2 mm. is an irregularly pear-shaped cavity 1.5 cm. long and varying from 1 to 7 mm. in breadth. This is filled with very dark blood. At numerous points the growth contains small bluish black areas, and at the point where the slit was noticed behind the cervix and from which the inky black blood escaped during operation there is a bluish black area, 4 x 3 mm. This opens directly into the vagina. The nearer one approaches the rectal attachment the more abundant become the bluish black areas.

The growth has also extended to the posterior vaginal wall. This near the cervix is 1 cm. thick. In the posterior vaginal wall at a point at least 1 cm. from the cervix is a cavity, 3 mm. long, filled with blood. At the upper end of the cervical stump is a hemorrhagic area, 3 mm. in diameter.

From a careful examination of the gross specimen it is clearly evident that we are dealing with a growth that occupies the posterior wall of the cervix and that has extended to and involved the outer coats of the anterior and lateral rectal walls, and has also extended to the vaginal mucosa posterior to the cervix. The tumor bears the definite earmarks of an adenomyoma of the recto-vaginal septum.

Histological Examination.—A very large section (Fig. 14) has been made taking in the entire cervix and a portion of the recto-vaginal growth seen in Fig. 13. The mucosa of the anterior vaginal wall is normal. The squamous epithelium of the vaginal portion of the cervix has in many places been rubbed off, but where present is normal. The mucosa lining the cervical canal is perfectly normal, but lying in the cervical canal is a small polyp consisting of mucosa of the type found in the body of the uterus.

The large irregular cyst noted in the posterior wall of the cervix is lined with one layer of low cylindrical epithelium. In some places this lies directly on the underlying fibrous tissue, but at other points is separated from it by a definite stroma. The cavity of the gland is partly filled with blood.

The growth occupying the posterior wall of the cervix and the anterior wall of the rectum consists of typical adenomyomatous tissue. The stroma of the cervix passes over imperceptibly into that of the growth, there being absolutely no line of demarcation. Scattered everywhere throughout this growth are large and small areas of uterine mucosa consisting of normal-looking glands embedded in the characteristic stroma of the mucosa. Here and there the glands are markedly dilated and filled with blood. As one approaches the rectum the muscle in places seems to be arranged circularly around bunches of glands. At some points, as is particularly well seen in Fig. 15, islands of uterine mucosa extend directly to the rectal mucosa.

In the posterior wall of the vagina just behind the cervix is an island of uterine mucosa which has opened directly into the vagina. It was from this point that the inky blood escaped during the operation.



FIG. 1.—An early adenomyoma of the recto-vaginal septum. (Case VI.)

Gyn.-Path. No. 22483. On vaginal examination a small hard nodule could be felt in the vaginal vault just behind the cervix. On opening the abdomen we found in the mid-line just below and behind the cervix a puckered scar, about 1 cm. in diameter. As will be noted in the picture, this had a striated arrangement. The ureters were dissected free and a complete hysterectomy was done.

For the histological picture of the puckered area see Fig. 2.



FIG. 2.—Adenomyoma of the recto-vaginal septum. (Case VI.)

Gyn.-Path. No. 22483. This is a section from the puckered area noted on the anterior wall of Douglas' pouch just below the cervix and shown in Fig. 1. The matrix of the section is composed of non-striated muscle and fibrous tissue. Occupying the center of the field are uterine glands surrounded by the characteristic stroma of the uterine mucosa. In the left lower corner is a miniature uterine cavity.

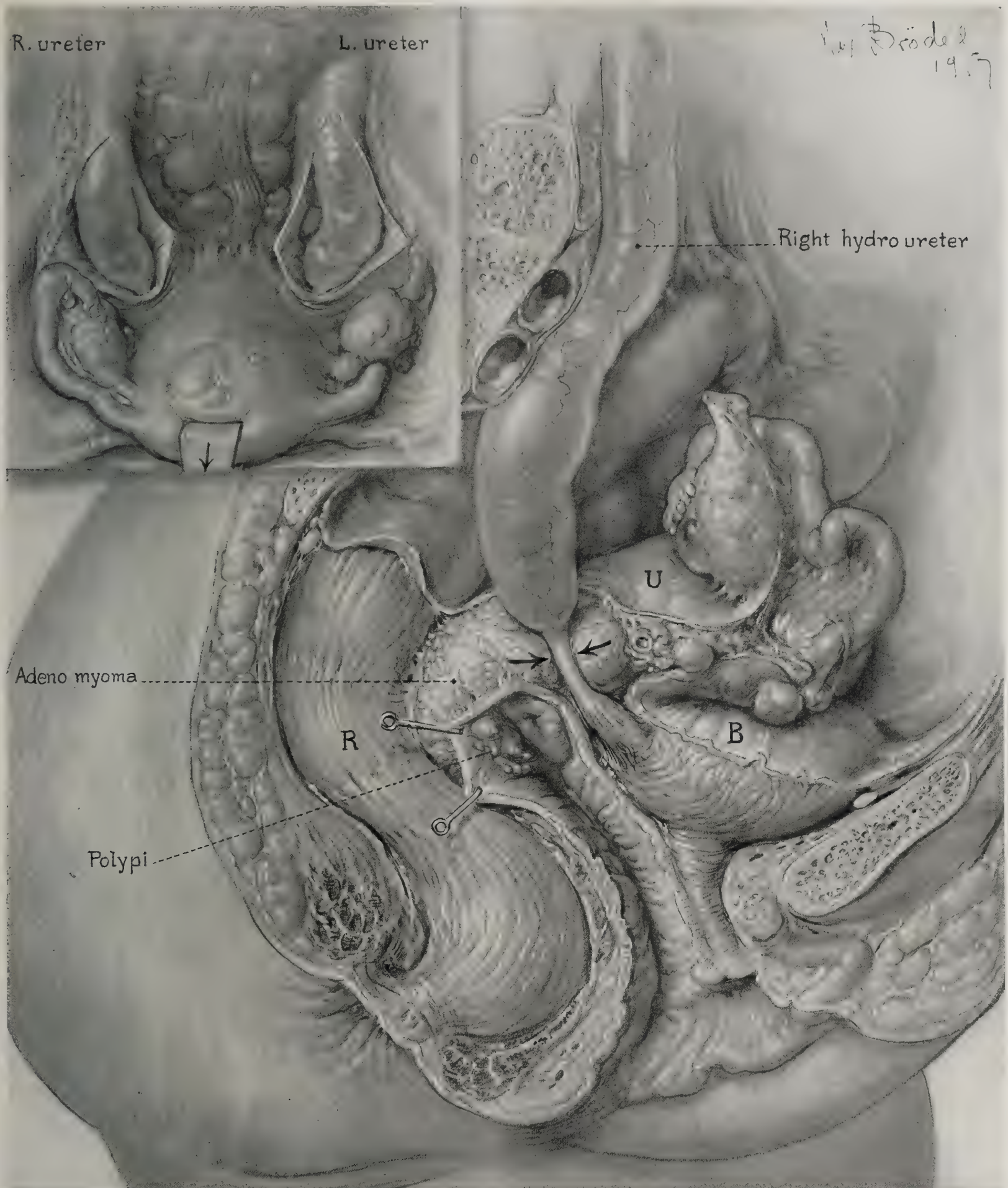


FIG. 3.—Dilatation of both ureters due to constriction by an adenomyoma of the recto-vaginal septum, which had extended out into the broad ligament on either side. (Case VII.)

In the left upper corner of the picture is shown the condition noted at operation. The rectum was firmly adherent to the posterior surface of the cervix. Both ureters were much dilated, being over 1 cm. in diameter.

The lower picture shows clearly the relation of the right ureter to the growth. The ureter is markedly dilated, but where it was encircled by the adenomyomatous tissue, as indicated by the arrows, it was greatly compressed, being not over 1.5 to 2 mm. in diameter. Near the bladder the ureter is slightly larger than normal.

The left ureter presented a precisely similar picture. At the menstrual period the adenomyomatous tissue evidently constricted the ureters still more, as is evidenced by the fact that during menstruation the patient had severe pain in both kidney regions.

The intimate blending of the growth occupying the posterior wall of the cervix with the anterior rectal wall is clearly seen. Behind the cervix the small polypi are seen projecting into the vagina.

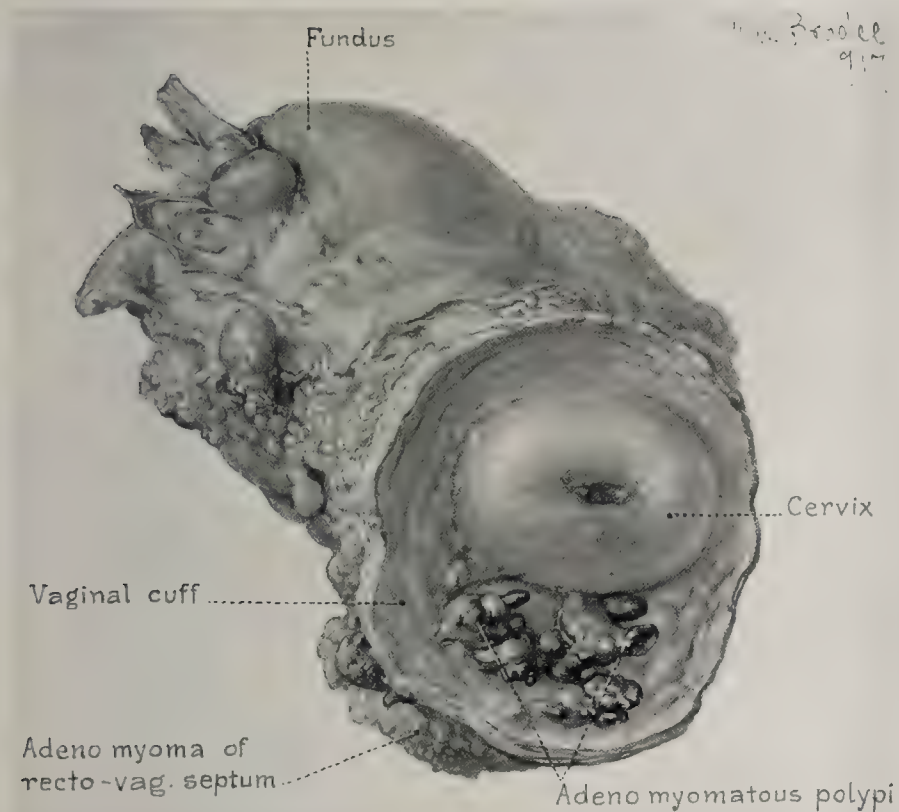


FIG. 4.—Adenomyoma of the recto-vaginal septum. Small adenomyomatous polypi projecting from the vaginal vault behind the cervix. (Case VII.)

Gyn.-Path. No. 23116. The uterus is little if at all enlarged. Springing from the side of the uterus are a few small myomatous nodules and attached to the surface are a few adhesions.

The vaginal portion of the cervix looks normal. Springing from the vaginal vault just posterior to the cervix are several polypi; some of these are blunt, others pointed. The majority of the polypi were bluish-black in color. These polypi were directly continuous with the adenomyomatous growth occupying the recto-vaginal septum. A portion of this recto-vaginal growth is seen. On account of the precarious condition of the patient time could not be taken to remove the rectal portion of the growth.

For the appearance of the growth on section see Fig. 5. For the histological picture consult Figs. 6, 7, 8, 9, 10, 11, 12.



FIG. 5.—Adenomyoma of the recto-vaginal septum with the formation of vaginal polypi. (Case VII.)

Gyn.-Path. No. 23116. This is a longitudinal section through the uterus shown in Fig. 4. Springing from the anterior surface of the uterus are a few small myomata and just above them are some adhesions. In the posterior wall of the fundus another small myoma is noted. The vaginal portion of the cervix, the mucosa lining the cervix and the cavity of the uterus are comparatively normal; the mucosa of the anterior vaginal wall is also unaltered.

Occupying a portion of the posterior wall of the cervix, the vaginal mucosa behind the cervix and extending to and involving the rectum is a diffuse striated growth. This contains dark, rather homogeneous areas. The growth also extends into the posterior vaginal vault forming blunt or pointed polypi.

For the low-power picture of the growth see Figs. 6, 10, 11. For the finer structures see Figs. 7, 8, 9.

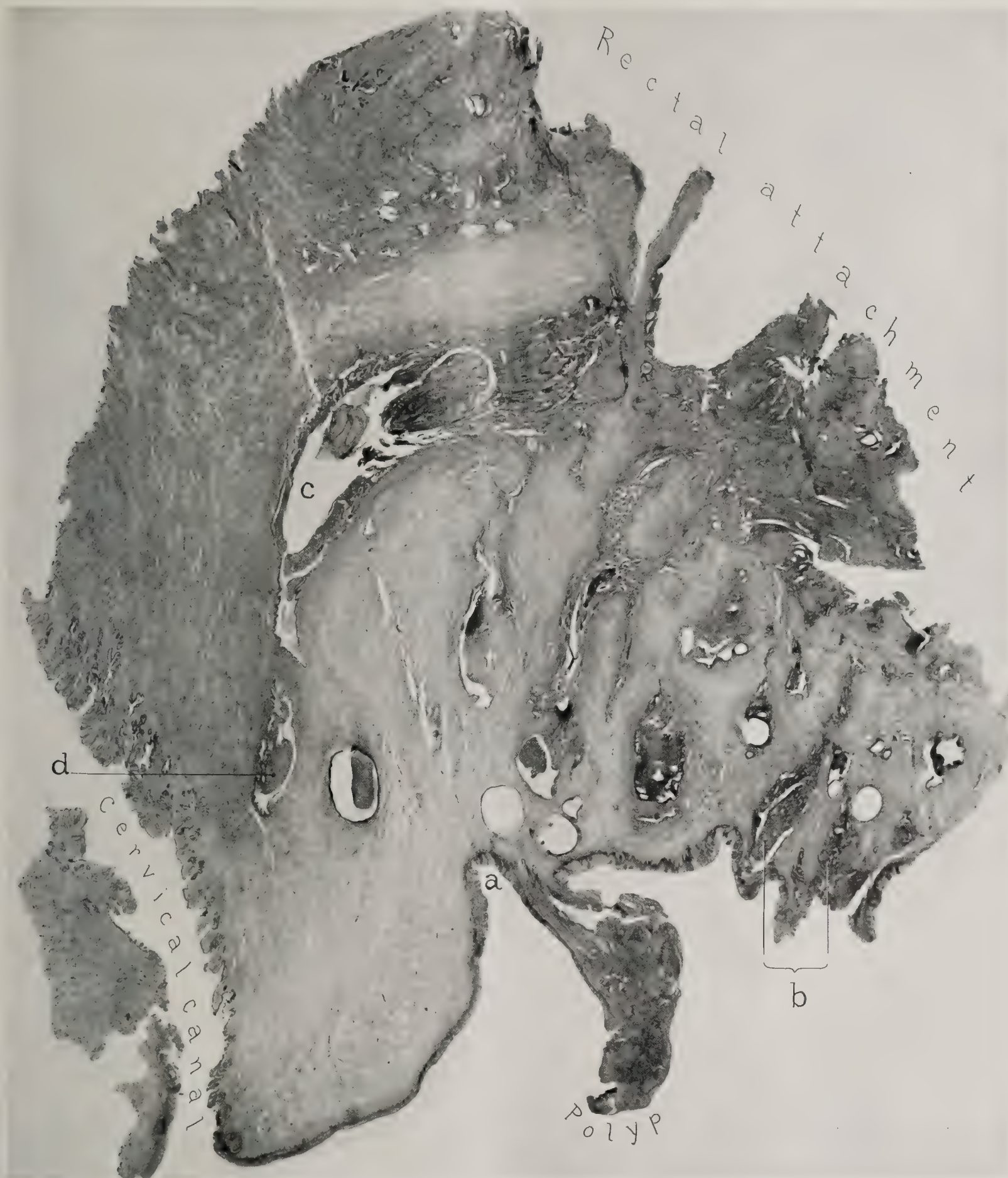


FIG. 6.—Adenomyoma of the recto-vaginal septum with the formation of vaginal polypi. (Case VII.)

Gyn.-Path. No. 23116. This is a low-power photomicrograph of the growth shown in Fig. 5. The section takes in a little of the mucosa of the anterior cervical wall and nearly all of that lining the posterior wall of the cervix. *a* represents the point where the cervix joins the vaginal mucosa.

The greater part of the picture consists of a striated growth with homogeneous areas scattered throughout it. Dotting these homogeneous areas are quantities of glands. Such areas consist of uterine mucosa identical with that normally found lining the cavity of the uterus. The nearer we approach the rectal attachment the more abundant are these islands or rivers of uterine mucosa.

At *a* a polyp is seen projecting into the vagina. This under the high power is seen to be covered over with vaginal mucous membrane, but scattered throughout its stroma are uterine glands.

At *b* the uterine mucosa has broken through into the vagina, the vagina at this point being lined with endometrium indistinguishable from that normally lining the cavity of the uterus.

At *c* is a miniature uterine cavity; at *d* a cervical gland is being distended by an area of normal endometrium. An enlargement of this area is shown in Fig. 9.

The rectal portion of the growth could not be removed on account of the precarious condition of the patient.



FIG. 7.—Adenomyoma of the recto-vaginal septum. (Case VII.)

Gyn.-Path. No. 23116. This is a higher magnification of some of the glandular areas seen in Fig. 6. From the left upper and right lower corners we get a fairly good idea of the stroma which consists of non-striated muscle and fibrous tissue.

Occupying the central portion of the picture are tubular glands lined with one layer of cylindrical epithelium and embedded in a stroma identical with that normally found in the mucosa lining the uterine cavity.

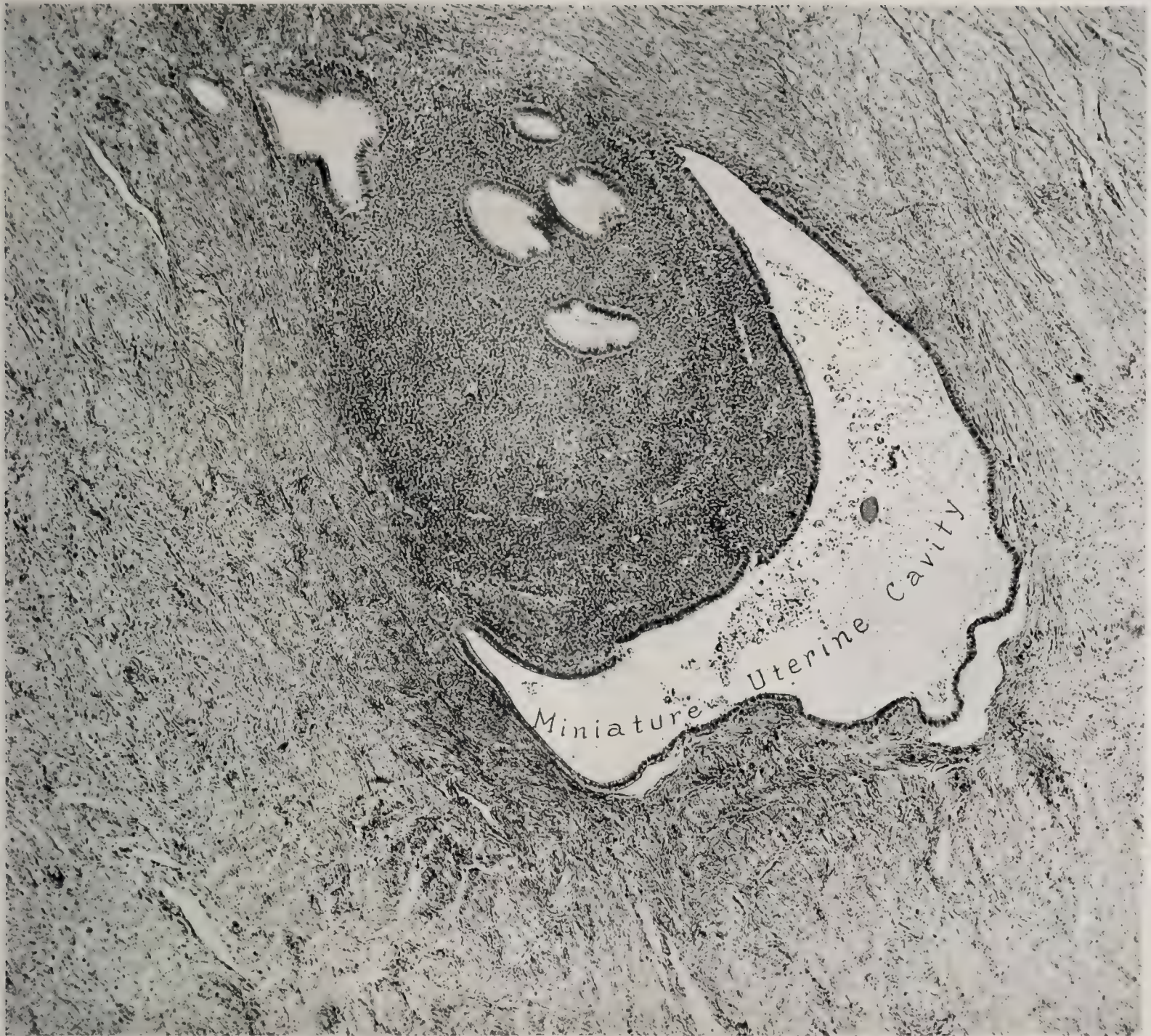


FIG. 8.—A miniature uterine cavity in an adenomyoma of the recto-vaginal septum. (Case VII.)

Gyn.-Path. No. 23116. Occupying the center of the picture is an area of typical uterine mucosa. It shows one layer of cylindrical epithelium and contains round or irregular glands lined with one layer of cylindrical epithelium. The glands lie embedded in an abundant and characteristic stroma.

This area drains into a miniature uterine cavity which contains exfoliated epithelium, leucocytes and shadows of red blood corpuscles, the remnants of old menstrual blood.

Surrounding this miniature uterine cavity with its adjacent mucosa is non-striated muscle.

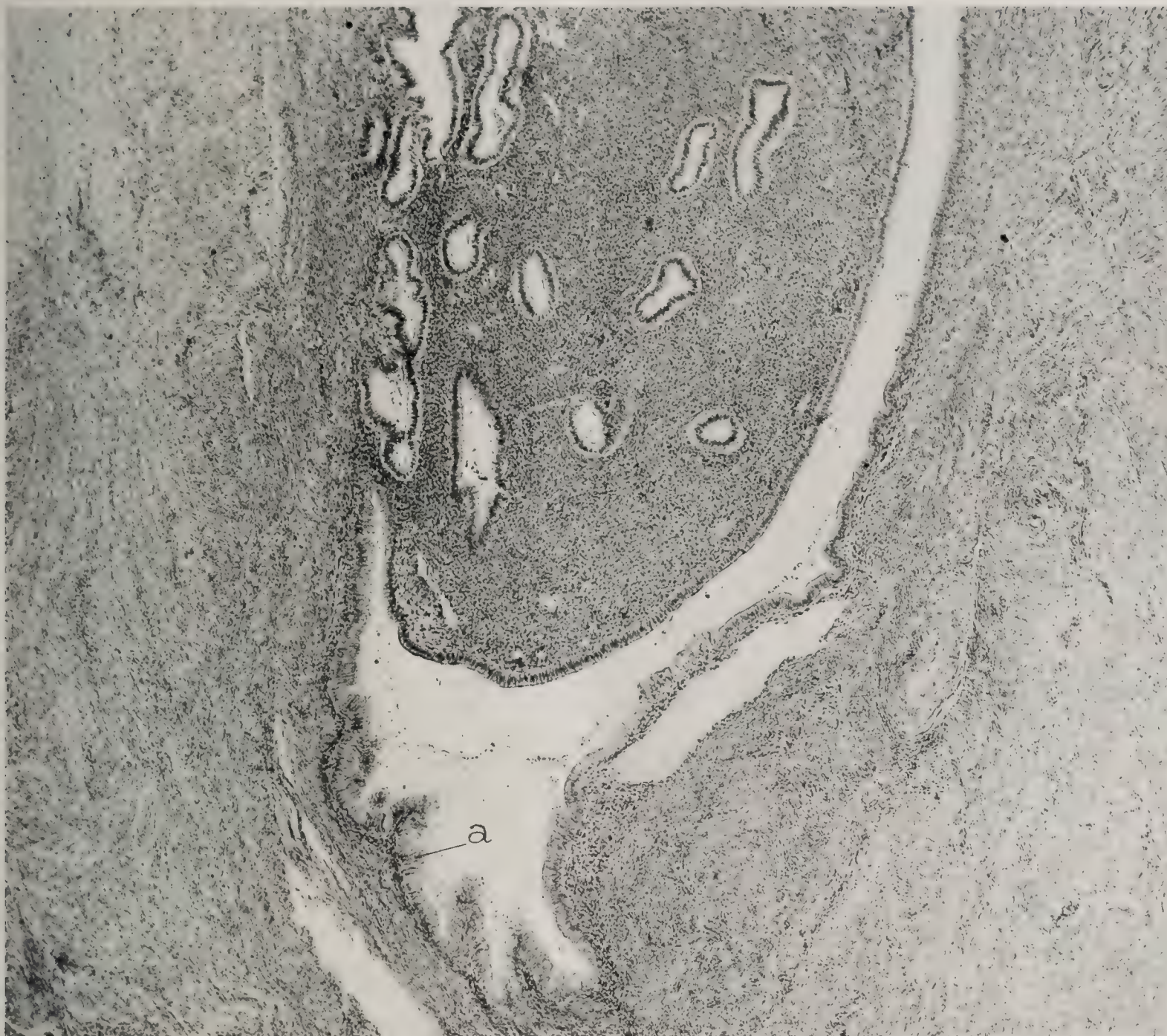


FIG. 9.—Adenomyoma of the recto-vaginal septum, an area of endometrium projecting into and distending a cervical gland. (Case VII.)

Gyn.-Path. No. 23116. This is an enlargement of the area *d* in Fig. 6.

Occupying the center of the field is an area of relatively normal endometrium, which is projecting into a cervical gland. The characteristic and very high cylindrical cells of the cervical gland are clearly seen at *a*. The cervical epithelium is playing no rôle in the development of the adenomyoma. Surrounding the mucosa is non-striated muscle and fibrous tissue.



FIG. 10.—An adenomyomatous polyp projecting into the vagina. (Case VII.)

Gyn.Path. No. 23116. The photomicrograph shows a portion of the posterior vaginal wall that was involved in the adenomyoma of the recto-vaginal septum. Scattered throughout the field are numerous areas of typical uterine mucosa and at *a* is a very large area of mucosa with a miniature uterine cavity.

The vaginal polyp which is one of those shown in Fig. 4 contains numerous glands. Its surface is covered with normal vaginal mucosa.

For the appearance of other vaginal polypi see Figs. 6, 11, 12.

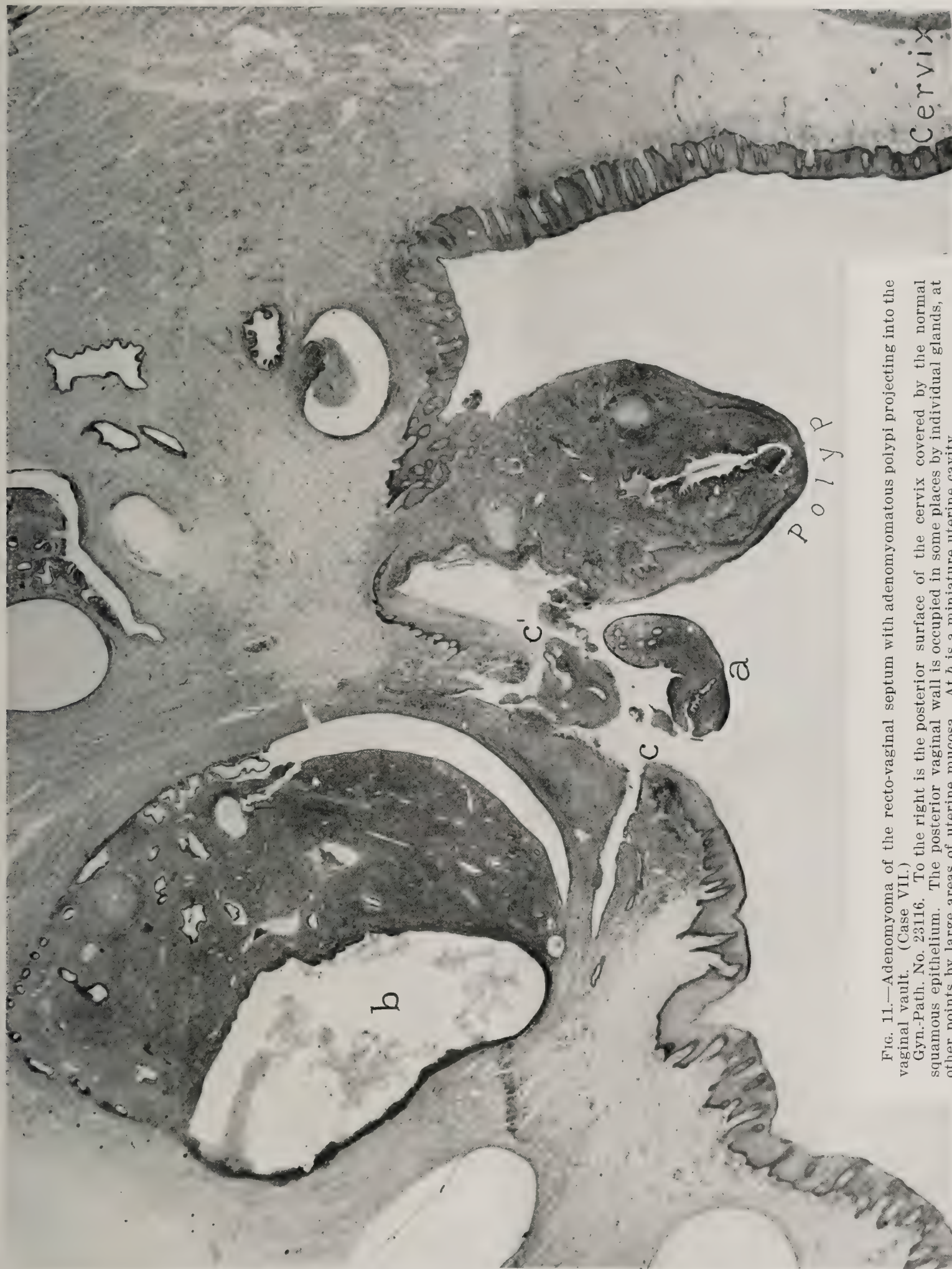


FIG. 11.—Adenomyoma of the recto-vaginal septum with adenomyomatous polypi projecting into the vaginal vault. (Case VII.)

Gyn.-Path. No. 23116. To the right is the posterior surface of the cervix covered by the normal squamous epithelium. The posterior vaginal wall is occupied in some places by individual glands, at other points by large areas of uterine mucosa. At *b* is a miniature uterine cavity.

Projecting into the vagina just behind the cervix is a polyp. This is covered with vaginal mucosa and in its interior are uterine glands.

Between *c* and *c'* the vaginal mucosa has been broken through and the uterine mucosa lines the vagina. Here also we have the uterine polyp *a*, which has an outer covering of one layer of cylindrical epithelium. Its interior consists of uterine glands embedded in their characteristic stroma. Menstrual blood undoubtedly escaped from this area at the period.

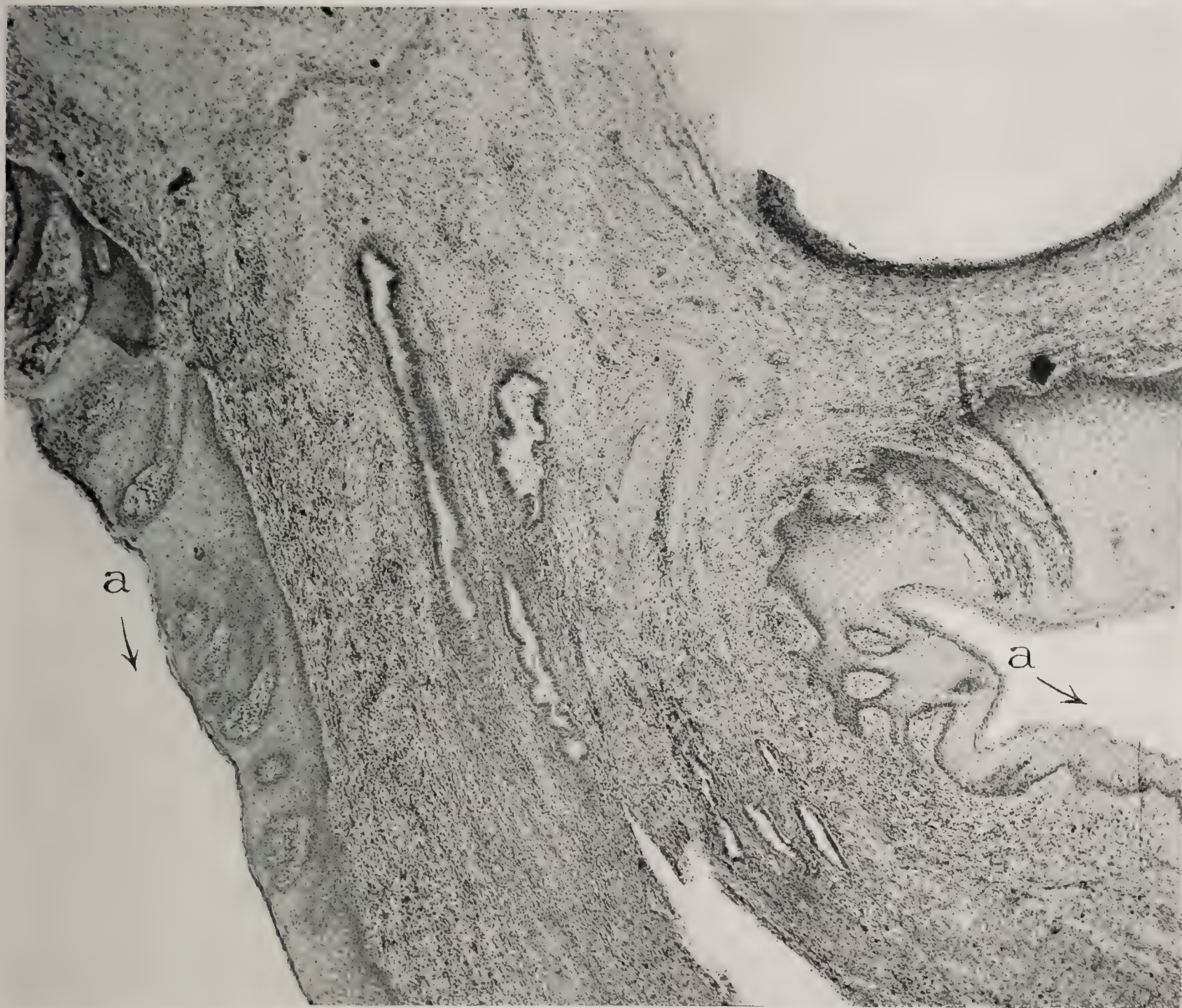


FIG. 12.—An adenomyomatous polyp projecting into the vagina. (Case VII.)
 Gyn.-Path. No. 23116. This is the base of one of the polypi seen in Fig. 6. The distance between *a* and *a* indicates the pedicle of the polyp and the arrows show the manner in which the polyp had spread out toward its tip.
 The vaginal mucosa is carried out over the surface of the polyp.
 The stroma of the polyp consists chiefly of fibrous tissue. There appears to be a small amount of non-striated muscle. Passing into the polyp from the underlying vaginal tissue are uterine glands.

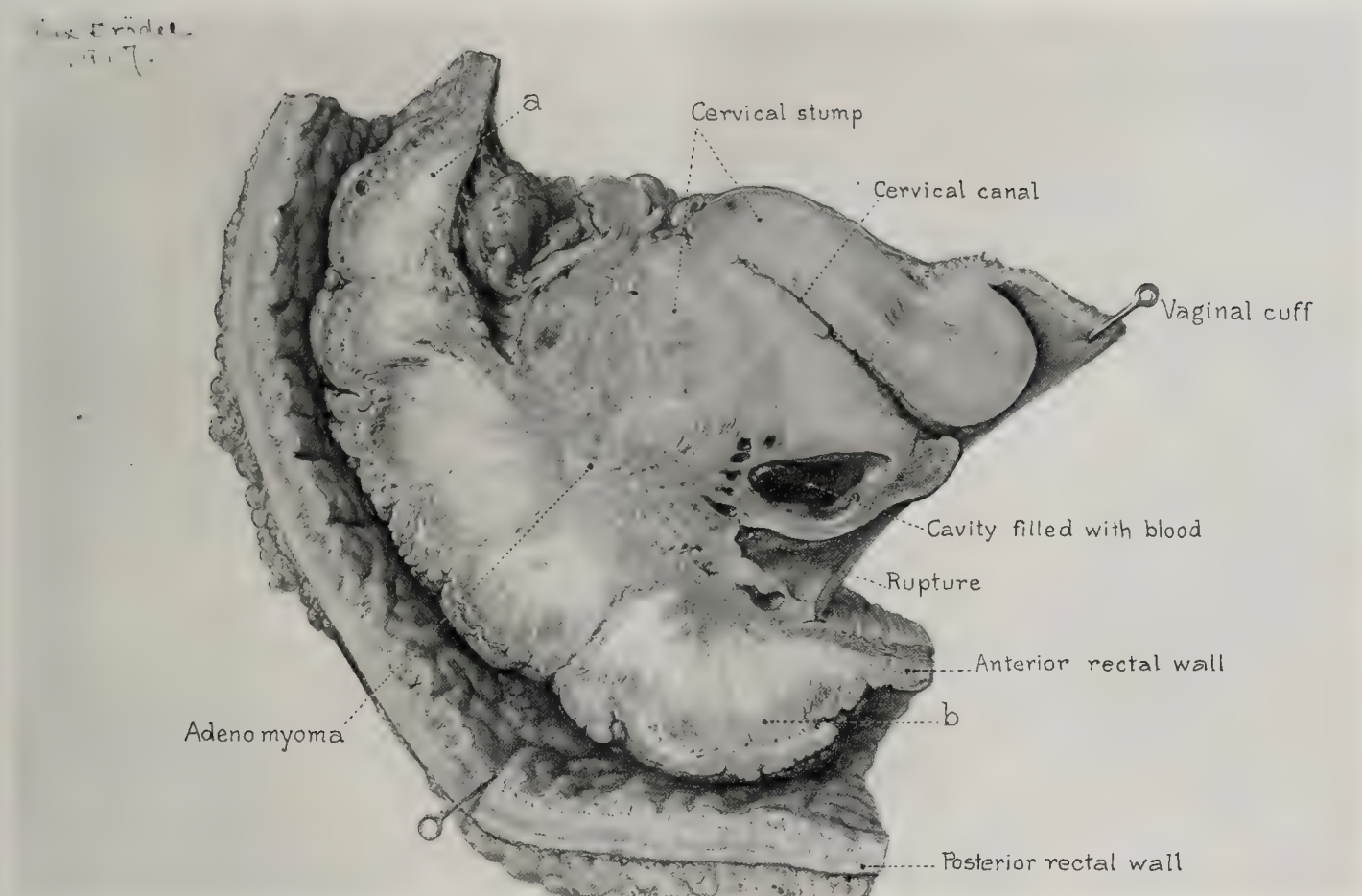


FIG. 13.—Adenomyoma of the recto-vaginal septum. (Case VIII.)

Gyn.-Path. No. 23074. The body of the uterus was removed for myoma two years ago. The specimen consists of the cervical stump and a greatly thickened segment of the adjacent rectum. The anterior vaginal wall is normal. The anterior lip of the cervix is unaltered and the cervical canal presents the usual picture.

In the posterior lip of the cervix is an irregular oval cystic cavity filled with blood. It was lined with one layer of low cylindrical epithelium which in some places rested on the stroma of the cervix. At other points, however, the epithelium rested on a very cellular stroma similar to that in the body of the uterus.

The posterior portion of the cervix has a coarse striated appearance and scattered throughout it are small, dark, cystic spaces. The cervical growth passes over imperceptibly into the greatly thickened anterior rectal wall. The rectal wall also presents a striated fibrous appearance particularly well seen at *b*. It is greatly thickened, in some places being nearly 2 cm. thick. The mucosa of the anterior rectal wall is intact, but here and there is gathered up into small polypi. The growth has also involved the lateral rectal walls. The posterior wall of the rectum is normal.

In the vaginal vault just behind the cervix a small cystic space opens directly into the vagina. It was from this point that the inky black blood escaped during the operation.

For the low-power picture of the cervix see Fig. 14; for the character of the rectal portion of the adenomyoma consult Fig. 15.

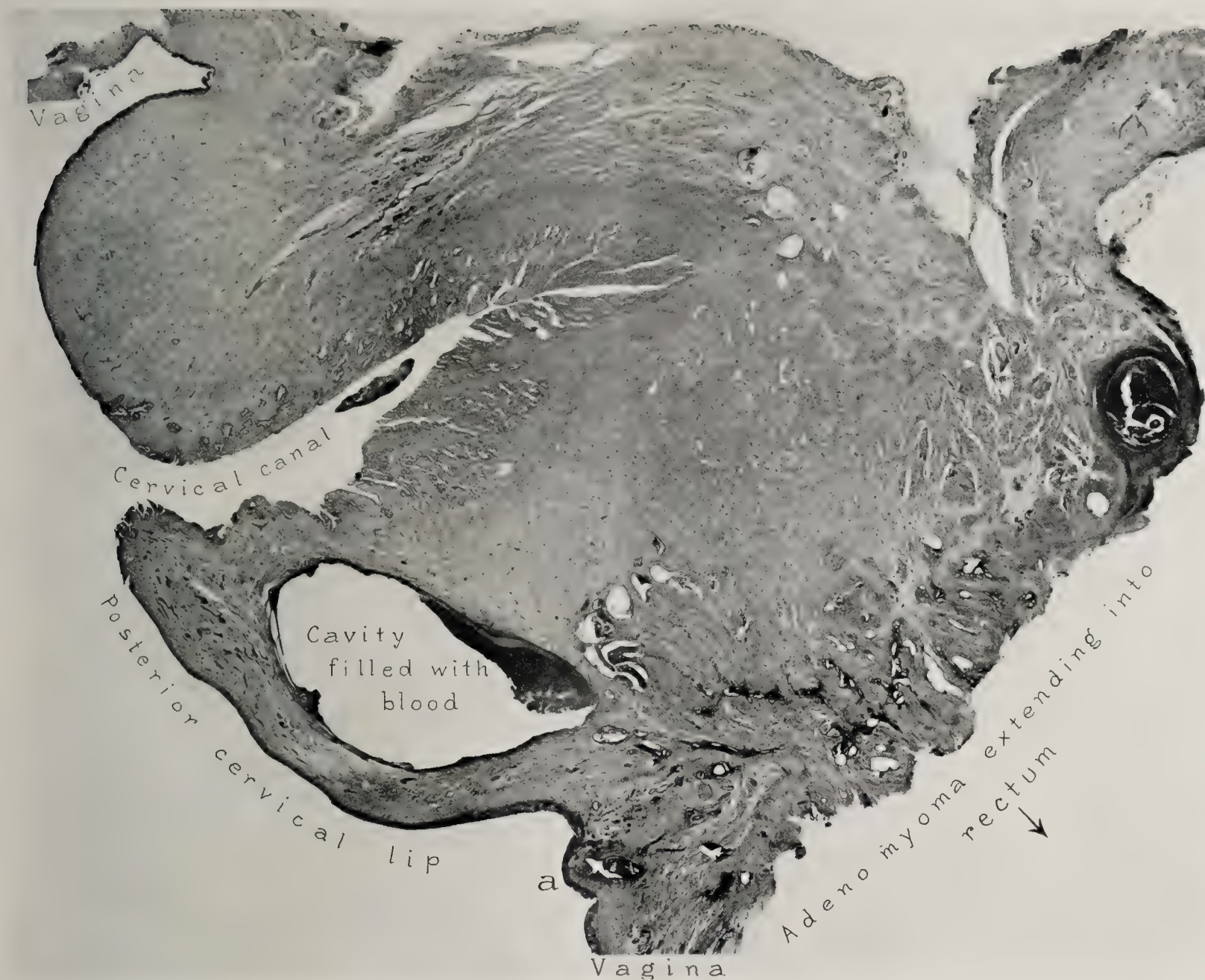


FIG. 14.—Adenomyoma of the recto-vaginal septum. (Case VIII.)

Gyn.-Path. No. 23074. This is a photomicrograph of the cervix—the body of the uterus had been removed two years before. The anterior wall of the cervix is normal. The mucosa lining the cervical canal presents the usual appearance, but lying in the canal is a longitudinal section of a small polyp.

The large cavity in the posterior wall of the cervix and noted in Fig. 13 was lined with cylindrical epithelium and was filled with blood.

Occupying the posterior part of the cervix is an adenomyomatous growth. It will be noted that the majority of the glands are embedded in a stroma; some of them are dilated.

It was at a point near *a* that the uterine mucosa had broken through into the vagina. From this point the inky black blood escaped during operation.

The widespread adenomyoma occupying the posterior part of the cervix was directly continuous with that involving the anterior and lateral rectal walls as indicated in Fig. 13. For the rectal involvement see Fig. 15.



FIG. 15.—Adenomyoma of the recto-vaginal septum encroaching on the rectal mucosa. (Case VIII.)
Gyn. Path. No. 23074. For the gross appearance of the specimen see Fig. 13.
This is a photomicrograph of a section from the anterior rectal wall. The rectal mucosa is normal, but immediately beneath it there is a diffuse myomatous thickening of the tissue and large quantities of normal-appearing uterine mucosa have invaded the rectal wall extending at one point almost to the rectal mucosa.

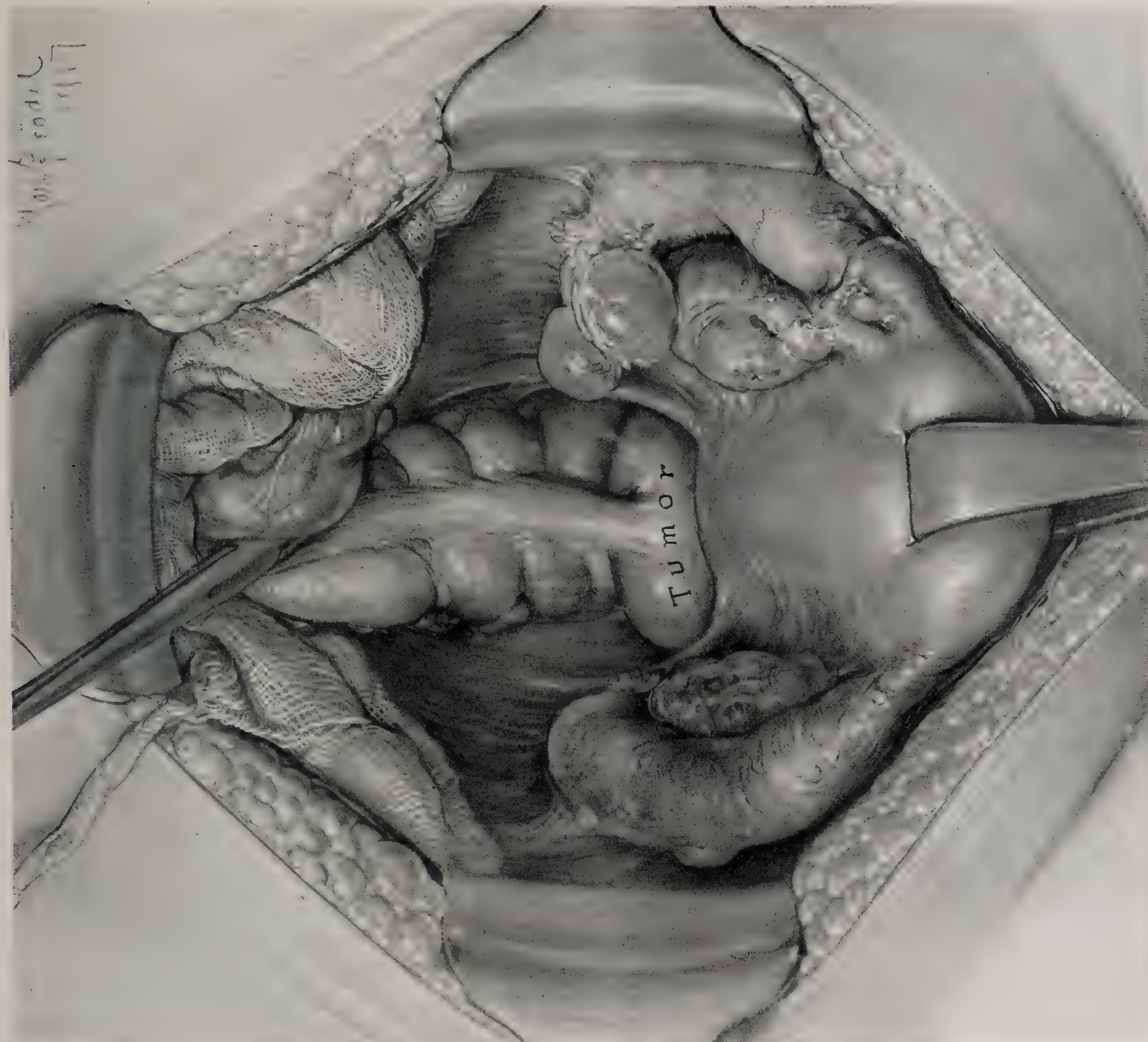


FIG. 17.—Adenomyoma of the recto-vaginal septum with the formation of sessile polypi in the vaginal vault: double pus tubes. (Case IX.)

Gyn. No. 22989. Both tubes are the seat of a pyosalpinx. Their fimbriated ends are slightly open, suggesting tuberculous (histological examination shows that they are tuberculous). Near the fimbriated end of the right tube are two small cysts. The ovaries are embedded in adhesions.

At a level of the internal os is a hard tumor, about 2.5 cm. broad. This involves the posterior surface of the cervix and the anterior surface of the rectum. For its appearance in the vaginal vault see Fig. 16.

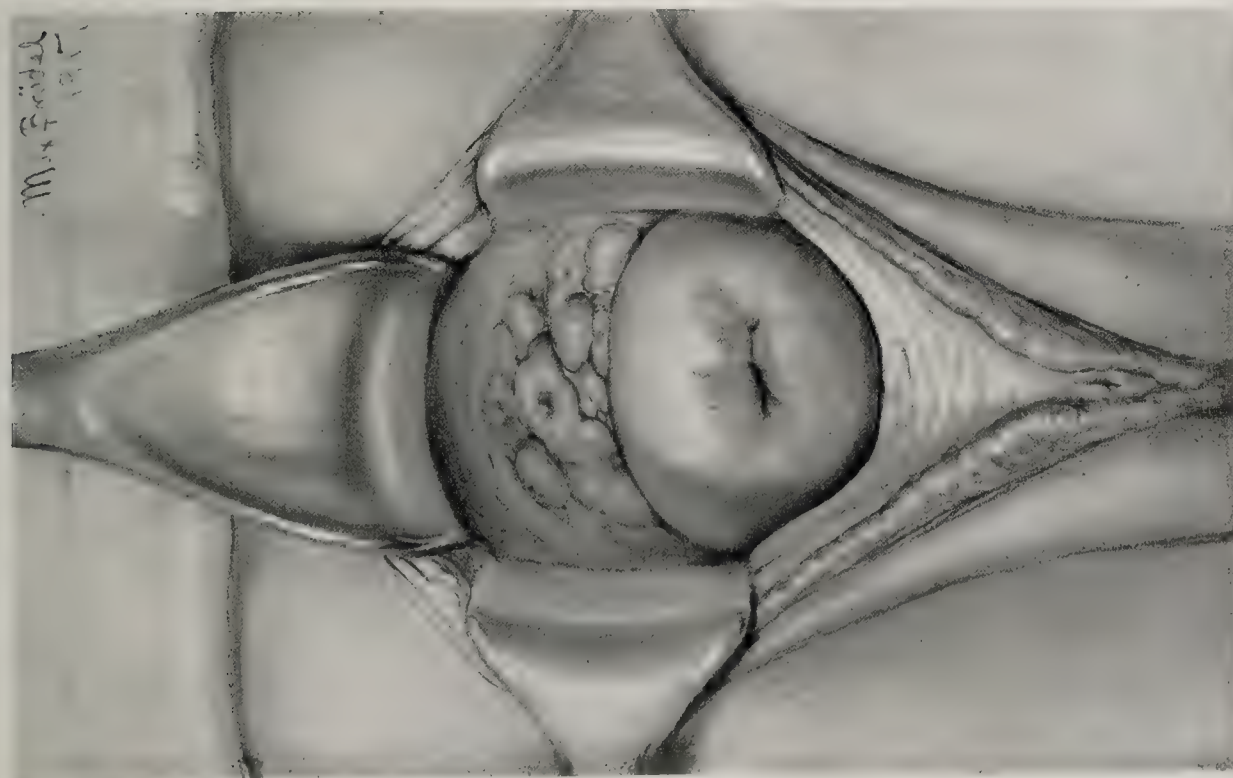


FIG. 16.—Sessile polypi in the posterior vaginal vault due to adenomyoma of the recto-vaginal septum. (Case IX.)

Gyn. No. 22989. The patient is in the knee-chest posture. The cervix is normal. The vaginal vault just behind the cervix presents a roughened, uneven appearance due to broad-based sessile polypi. These are smooth and are covered over with vaginal mucosa. At several points there were small, brownish cystic areas in the polypi, evidently due to old menstrual blood that had accumulated in the substance of the polypi.

The growth extended through to and involved the anterior rectal wall (see Fig. 17).

Later on we expect to remove the uterus, posterior vaginal vault and the involved area of the anterior rectal wall.

No histological examination of the tumor has as yet been made, but the diagnosis is perfectly clear.

We have in this case had the opportunity of examining the patient from time to time during the last ten years. Ten years ago a subperitoneal myoma was removed during pregnancy; two years ago Dr. Stavely did a supravaginal hysterectomy for myoma. At that time there was no evidence of an adenomyoma of the recto-vaginal septum nor were there any clinical manifestations of such a condition except pain on defecation. No thickening could be detected, consequently we must conclude that this widespread growth has developed in large measure or entirely during the last two years.

CASE 9.—*Adenomyoma of the recto-vaginal septum with the formation of polypi in the vaginal vault; double pus tubes (tuberculous).*

Gyn. No. 22989.—M. W., aged 28, married, was admitted to The Johns Hopkins Hospital on April 17, 1917. The patient is a well-nourished colored woman. She complains of pain in the lower abdomen.

Her menses began at eleven, were regular, lasted three days, were free and painless. For the last four or five years, however, she has had some pain at the period. She menstruated on February 25, and since then has had slight bleeding from time to time, lasting, however, only a few hours. She missed her period in March but for the last two days has been bleeding constantly and rather profusely.

During February urination was frequent and painful and she had to void two or three times each night. At present there is no discomfort on micturition. Recently she has had a good deal of tenderness in the right lower abdomen. Her leucocyte count is 7000; her hæmoglobin 52 per cent.

She has been married eight years but has never been pregnant.

The outlet is moderately relaxed. Bartholin's glands are not felt and there is no urethral reddening. The cervix is normal in size. Its mobility is somewhat restricted and manipulation of the cervix causes pain.

There is marked induration in the vaginal vault behind the cervix, and on exposing the vagina we see the condition shown in Fig. 16. The posterior vaginal vault presents an uneven and puckered appearance due to numerous rather flat, smooth, sessile polypi. These are everywhere covered over by vaginal mucosa but some of them are slightly cystic, and in the depth of a few a definite brownish color is clearly demonstrable making the diagnosis of adenomyoma certain. There is a considerable amount of induration in both vaginal fornices.

On rectal examination a bar of indurated tissue, at least 2 cm. in width, is felt between the rectum and cervix. The rectal mucosa itself is intact and smooth, but small, hard, shot-like masses can be felt in the rectal wall above the growth. These are not larger than split peas. Proctoscopic examination reveals a normal-looking mucosa.

Operation, April 23, 1917.—On opening the abdomen I found the picture shown in Fig. 17. Each tube was the seat of a pyosalpinx,

but the fimbriated ends of both tubes were slightly open, strongly suggesting tuberculosis. We thought it wiser to remove the tubes before removing the uterus thus reducing to the minimum the chances of infection. The ovaries were also removed, in the first place because they were densely adherent, in the second place because if any portion of the adenomyoma were left behind the presence of the ovaries would tend to stimulate the further extension of the portions of the tumor that it had not been possible to remove.

After removal of the appendages we carefully examined the uterus and rectum. In the posterior wall of the uterus was a subserous myoma 1 cm. in diameter. Behind the cervix at the level of the internal os was a hard indurated mass, 2.5 cm. in diameter. This involved the posterior wall of the cervix and the anterior wall of the rectum (Fig. 17). The bowel wall and the uterine wall at this point were intimately blended together. It was perfectly clear that we were dealing with an adenomyoma of the recto-vaginal septum.

The patient's pulse was very rapid before the operation was started and by the time the tubes and ovaries had been removed was varying from 160 to 170; consequently it was deemed safer to defer the hysterectomy until a later date. A pulse of from 140 to 160 is frequently encountered during an operation for pus tubes and as a rule occasions no alarm, but the patient could not have withstood the widespread dissection and the hysterectomy that would have been necessary.

She had a stormy time for the first three days, but then improved rapidly. She was discharged on May 6 with instructions to return several months later for removal of the recto-vaginal growth.

This growth on histological examination will undoubtedly show the typical adenomyomatous picture. Its situation is characteristic and the picture as seen in Douglas' cul-de-sac further substantiates the diagnosis. The development of the flat polypoid condition in the vaginal vault is also confirmatory, and the brownish hue due to the accumulation of old menstrual blood in the polypi leaves no doubt as to the presence of adenomyoma. As was noted the rectal mucosa itself was normal.

Gyn.-Path. No. 23170.—Sections from the Fallopian tubes show typical tuberculosis.

It is a pleasure to acknowledge my obligation to three of my friends who have added greatly to the value of this article. Mr. Max Brödel, the Director of the Department of Art in Medicine in The Johns Hopkins Medical School made the drawings which so faithfully portray the conditions found. Dr. Benj. O. McCleary took infinite pains in the making of very large sections which included the cervix and a portion of the rectum in one piece. Mr. Herman Schapiro has furnished us with photomicrographs which it would be almost impossible to excel.

HEMATOMATA OF THE OVARY, INCLUDING CORPUS LUTEUM CYSTS.*

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There is no organ in the body which is so frequently the seat of hemorrhages as is the ovary. Indeed, so common are they that no clinical significance is attached to the small

hematomata so frequently found in the ovaries removed at operation. In the case of large blood tumors, the clinical picture is essentially that which characterizes other benign ovarian neoplasms.

That even small hematomata are not altogether without important clinical potentialities is shown by the fact that

* Read before The Johns Hopkins Hospital Medical Society, May 7, 1917.

they may give rise to serious and even fatal hemorrhage into the pelvic and abdominal cavities, as I have shown in a recent paper.¹ In this I collected 39 previous cases of grave abdominal hemorrhage of ovarian origin, and reported a fortieth in which the hemorrhage was due to the rupture of a small follicular cyst of the ovary.

Aside from such extreme instances of what may be called perforative ovarian hemorrhage, great interest attaches to the study of hemorrhages which are confined within the ovary. Considering the great frequency of ovarian hemorrhages, it seems difficult to assume that their occurrence can be looked upon as being invariably pathological. In view of the physiological nature of the hemorrhage which occurs periodically from the uterus, *i. e.*, the menstrual flow, it does not seem impossible that the study of ovarian hemorrhage may perhaps throw some light on the still mysterious mechanism of menstruation and ovulation. A number of studies have been made of the subject of ovarian hematomata, but there has been no effort, so far as I have been able to learn, to study them from the viewpoint of the physiological functions of the ovaries.

The material upon which this study is based was derived from 85 cases in which one or both ovaries had been removed at operation. Some of these ovaries contained only one hematoma, some a great many. The selection of this material was made relatively simple by the obviousness of hematomata on naked eye examination. I need not say that in all cases the ovaries were cut into at various planes, for the surface appearance of an ovary is of little importance as an index of its internal structure. The study has aimed to include all hemorrhagic lesions encountered, so that the series includes small follicular hemorrhages as well as the larger hematomata of pseudo-neoplastic type. In other words, it was not limited to the comparatively small group in which the blood tumor was so large as to give rise to the symptoms which indicated operation. By far the largest proportion of hematomata studied, as a matter of fact, were quite small, not exceeding 2 cm. in diameter. These smaller lesions afford a much better opportunity than the more extensive ones of solving the important question of pathogenesis. The largest hematoma in this series measured 6 cm. in its longest diameter. Larger ones than this are relatively rare.

Hematomata of the ovary have been variously classified. We are not here concerned with those rare forms of ovarian hemorrhage that are produced by such conditions as a ruptured ovarian pregnancy, rupture of ovarian varices, bleeding from malignant ovarian tumors, etc. Nor are we concerned with the incidental hemorrhages which often occur into large ovarian cysts. The more intrinsic forms of ovarian hemorrhage, with which this paper deals, are classified by Von Beust² into those occurring in the stroma of the ovary, those in the follicles and those in the corpora lutea. Wolf's³ division, which seems less logical, is into the interstitial, follicular and intra-follicular varieties. This classification is practically the same as that of Pfannenstiel.⁴ Klob⁵ recognizes only follicular and parenchymatous forms of hemorrhage, speaking

of the latter as "ovarian apoplexy." Rollin's⁶ classification, so often quoted, would seem to be the most complex and least satisfactory of all. He subdivides ovarian hemorrhages into (1) multiple vesicular, in which a number of follicles are filled with blood; (2) extravascular, in which the hemorrhage has broken into the abdominal cavity; (3) intravascular, in which the follicle wall resists the pressure of the blood, so that a large hematoma is formed; (4) hemorrhage into a hydropic follicle, the contents being a sanguinolent fluid instead of pure blood; (5) hemorrhage into a corpus luteum. The classifications suggested by other authors (Oehman,⁷ Savage⁸ and others) differ in no important respect from those already quoted.

In investigating the material on which this paper is based, I was impressed by the fact that, in the overwhelming proportion of cases, hematomata of the ovary are the result of hemorrhage into the follicular structures, including under this head the corpus luteum, which is a derivative of the Graafian follicle.

For a proper understanding of the pathogenesis of ovarian hematomata, the first essential is a knowledge of the blood supply of the Graafian follicle and of the corpus luteum. The vascular supply of the maturing follicle is found in its theca interna, the vessels of which form a veritable wreath around the follicle. From this, tiny vessels make their way concentrically inward toward the granulosa, in which, however, no distinct vascular channels can ordinarily be made out. It has now been fairly well established that the discharge of the ovum occurs without any appreciable bleeding either into the abdominal cavity or into the follicle lumen. Following the rupture of the follicle, *i. e.*, in the earliest stages of the corpus luteum, there becomes evident a much richer development of the blood supply, so that this early stage in the life history of the corpus luteum is often spoken of as the stage of hyperemia. Not only do the vessels in the theca become larger and more numerous, but within this, at the base of the granulosa, which it thus marks off from the theca, there appears a delicate festoon of small vessels which completely surrounds the corpus, forming a rather striking line of demarcation between granulosa and theca. This subgranulosal vascular wreath is of great importance, because from it spring the capillary channels which later irrigate the granulosa cells, coincidentally with the lutein transformation of the latter. Once the lutein layer is well established the subgranulosal vascular wreath becomes less conspicuous. The thecal stratum of blood vessels, however, appears to be quite distinct throughout the active life of the corpus luteum, and even well into the period of retrogression.

Furthermore, it is usually quite definite in those follicles whose development becomes arrested at various stages, through the process known as atresia folliculi—a term which seems to have become generally accepted in spite of the fact that it is far from satisfactory. As is now well known, only one follicle each month undergoes full maturation, followed by rupture and the development of a corpus luteum. Many more, however, develop up to a certain point, at which their further

growth is inhibited by some influence, as yet unknown, but which probably emanates from the "presiding ovum" of the month. The arrest of follicular development is characterized by the death and disappearance of the ovum in the atretic follicle, together with a gradual disintegration of the membrana granulosa. It is thus easy to explain the various types of follicular cyst which are so commonly encountered clinically. For example, the small microscopic cyst with perhaps a single layer of low cuboidal epithelium represents a follicle blighted in its very early stages. The larger cyst cavities, with several layers of lining epithelium, correspond to follicles whose development has been inhibited after they have progressed well on toward complete maturity. Again, the cavities in which the surrounding epithelium has long since disappeared, and which are undergoing a genuine atresia by the formation of a cicatrix-like inner layer of fibrous tissue, represent very late stages, illustrative of the ultimate fate of the atretic follicles. The terminal product is the so-called corpus fibrosum, which it would seem well to distinguish from the corpus albicans, the end result of the corpus luteum.

The more important elements of the ovary are therefore all of follicular origin, namely, the Graafian follicle itself, the atretic follicle and the corpus luteum. The last-named is so specialized in function that it deserves separate consideration. Hemorrhage may occur in any one of the structures already enumerated, and also occasionally in the stroma of the ovary itself. The various forms of ovarian hematoma may thus be classified as follows:

Follicular	{	Graafian follicle.
		Atretic follicle.
		Corpus luteum.
		Stromal.

Hemorrhage into the Graafian Follicle.—Although practically all writers speak of the possibility of hematoma arising from hemorrhage into the Graafian follicle, it is my impression that this form of follicular hemorrhage is not by any means so common as has been believed. Practically every ovary during reproductive life contains many follicles which show degrees of development varying from the primordial follicle up to the fully mature structure. All of these advancing follicles, however, are characterized by relatively thick walls and by a moderate degree of thecal vascularity. The only exception to this is found in the case of the one follicle which is, as it were, chosen for full fruition and rupture each month. This follicle is larger and possesses a much richer blood supply than those which it has outstripped in development, although its walls are certainly much less vascular than those of the early corpus luteum. For the above reasons it is difficult to imagine that hemorrhage into a virile Graafian follicle would be common, except perhaps in the mature or almost mature forms. Even if such hemorrhage does occur, it is not easy to distinguish it histologically from the more usual type of hemorrhage into atretic follicles. In the former the hemorrhage brings about the death of the ovum, whereas in the latter the ovum has disappeared before the hemorrhage has occurred. It would not be possible to

distinguish these two histologically except in the few instances in which sections are obtained showing hemorrhage into follicles still containing the ovum and discus proligerus, *i. e.*, before the ovum has been destroyed.

Hemorrhage into Atretic Follicles.—This is the most frequent form of follicular hemorrhage. The condition of the ovary commonly spoken of as cystic degeneration is caused by a marked stimulation of the ripening process in many follicles, resulting in the formation of a large number of atretic follicles, clinically termed follicular cysts. It is extremely common to find that a greater or less number of these cystic follicles are the seat of hemorrhage, giving rise to the most frequent form of follicular hematoma. It is of interest to study the pathogenesis of this form of hematoma. The atretic follicle is usually lined with only one layer of epithelium; and in the later stages this also disappears. In the cystic stage, therefore, before the process of atretic obliteration has begun, it is usually a thin-walled structure containing fluid under a considerable degree of tension, as may be judged by the smooth outline of its wall. Surrounding the follicle is the theca with a vascular wreath. The point to be emphasized is the richness of this blood supply, in view of the fact that the atretic follicle is looked upon as a retrogressive structure. The veins especially are large and distended. That this is not a mere stasis or pressure hyperemia would seem to be indicated by the fact that only certain types of atretic follicle are thus characterized, and that, as I shall show later, it is only at certain stages of the menstrual cycle that this change is noted.

It can be easily understood that this perifollicular wreath of thin-walled veins is an important predisposing factor to hemorrhage. Primarily this hemorrhage is practically always perifollicular. Extensive extravasations of blood are frequently observed surrounding large segments of the follicle, often dissecting away the epithelium and causing great bulging into the lumen. Fig. 1 shows such a perifollicular hemorrhage with impending rupture into the cavity. Fig. 2 illustrates the next stage, in which the epithelium has just been broken through, the blood now filling the cavity. In the case of the large follicular cysts into which free hemorrhage takes place, it is evident that large ovarian hematomata may be formed. More commonly, of course, the atretic follicle is small and the hemorrhage not great, so that the resulting hematoma is of small size. The bleeding from the wall is often so slight that the cavity is only partially filled (Fig. 2). Not infrequently the bleeding seems to have recurred, perhaps a number of times, the extravasated blood in the lumen being given a ripple-like appearance. Sometimes rather large hematomata may be caused by the confluence of two or more adjacent ones.

These observations would seem to refute the views of Savage and others that hemorrhage into the stroma is secondary to hemorrhage within the follicle, the blood escaping from the latter when the tension ruptures the wall. The present study would indicate that the real process is just the reverse, that is, the primary hemorrhage occurs in the perifollicular stroma and later breaks through into the follicle.

It is not always easy to distinguish this form of follicular hematoma from genuine stromal hemorrhage, on the one hand, and hemorrhage into corpora lutea, on the other, even with the aid of the microscope. A non-follicular stromal hemorrhage may be surrounded by a condensed layer of fibrous tissue quite similar to the wall of an atretic follicle from which the epithelium has perhaps long since disappeared. Equally perplexing may be the differentiation between simple follicular hematoma and that which arises in a corpus luteum. As is now well known, the theca cells of the atretic follicle often undergo a definite lutein-like transformation, and hemorrhage into a follicle surrounded by a zone of these theca-lutein cells is not always easy to distinguish from an old corpus luteum hematoma in which the lutein cells have undergone marked retrogression.

Corpus Luteum Hematoma.—For a proper understanding of the histology of hematomata of this type, a knowledge of the life history of the corpus luteum is essential. This I have described elsewhere,⁹ and I shall not review it here. Contrary to what has been the common belief, it is not characteristic to find the cavity of the follicle filled with blood immediately after its rupture. The walls of the corpus luteum in these very early stages, however, are very vascular, the subgranulosa vascular ring being especially marked. There is no dividing line between this stage and that of vascularization. As a matter of fact, it is common for the early corpus luteum to exhibit the hyperemic stage in some parts of its wall, while others have passed on into the stage of vascularization. In the latter the lutein layer becomes thickly irrigated with capillaries springing from the subgranulosa zone. It is in this time period of the corpus luteum that a moderate amount of hemorrhage normally takes place into the lumen. It is found in all the corpora lutea of this stage that I have examined. The hemorrhage is moderate in amount and usually uniform in distribution, the escaped blood forming a narrow zone adhering to the inner layer of the lutein zone.

It is not surprising, however, that in certain instances this hemorrhage overshoots the mark, as it were, the cavity of the corpus being inundated. Thus is produced one very common form of what is clinically called a corpus luteum cyst (Fig. 3). The statement has generally been made that corpus luteum cysts invariably contain blood. With certain qualifications which will be discussed later, this statement is correct.

Many of the structures which the gynecologist speaks of as corpus luteum cysts are merely corpora lutea in which an unusual amount of bleeding has occurred. It is probable that in many of these the lutein cells remain virile and functionate normally, and that the abnormal amount of hemorrhage has no important effect on the subsequent history of the corpus luteum. In other cases it is conceivable that the hemorrhage may be so great that the further development of the functioning cells is arrested and that a genuinely pathological hematoma results. There is no sharp dividing line between the physiological and the pathological in this respect, any more than there is between the uterine bleeding of normal menstruation and that which constitutes menorrhagia.

Hemorrhage from the wall of a corpus luteum in the stage of maturity is probably rare. The walls of such a corpus are usually very thick, the blood vessels are thick-walled and lie more deeply, and there is a more or less well-defined layer of fibrous tissue along the inner edge of the lutein zone. Even if excessive hemorrhage occurred in this stage it would seem impossible to distinguish the resulting hematoma from the usual type already described, in which the hemorrhage arises during the stage of vascularization, and in which the wall later undergoes the same maturation observed in the normal corpus (Fig. 4). In a certain number of hematomata, which because of their yellow lining are clinically called corpus luteum cysts, the walls are found to be those of retrogressive corpora lutea. In these cases, for reasons similar to those above mentioned, it is almost certain that the initial bleeding occurred in the stage of vascularization, and that the blood has persisted to the period of retrogression of the follicle. This is not surprising when one considers that the entire time elapsing between the periods of late vascularization and early retrogression of the corpus luteum may be little more than a week.

The especial characteristic of old corpus luteum cysts is the fact that the lutein layer is atrophic and degenerated, and that it is separated from the lumen by a distinct and often wide zone of connective tissue (Fig. 5). The contents are usually old blood. Instead of filling the cavity completely, the hemorrhagic elements often form only a narrow layer adhering to the wall of the cyst, the remainder being a clear serous fluid. This type of cyst is very common. It is certainly a pathological structure, although its clinical significance is often negligible.

The multiple lutein cysts which are at times found in the ovaries in association with either hydatidiform mole or chorio-epithelioma, and which contain no blood, need not be considered at length here, inasmuch as they are not corpus luteum cysts in the proper sense. The lutein cells which are found in the walls of these cysts are theca lutein cells and not granulosa lutein cells. Even in the course of normal pregnancy there is a great overproduction of atretic follicles, with a lutein-like transformation of the theca interna cells, giving rise to the so-called interstitial glands. It seems impossible to explain this in any other way than as due to a hormone emanating from the embryo. When the latter is pathological, as in hydatidiform mole or chorio-epithelioma, it is not surprising that there should also be a pathological condition in the ovary. Since in both these conditions, there is an overproduction of trophoblastic tissue, the thought suggests itself that the hormone which is linked up with ovarian activity is produced by the trophoblast, and that the excess of the latter in these two diseases is responsible for the remarkable polycystic lesions which may occur in the ovary. In the two specimens of this condition which I have had an opportunity of studying, the lutein cysts presented a picture quite different from the ordinary corpus luteum cyst. The lutein cells rarely form a complete or uniform layer. They are usually large, more or less polyhedral, taking a rather purplish hematoxylin stain. The lutein zone is often buried beneath a deep stratum of

fibrous tissue, indicating that the atretic follicle in which this lutein transformation of the theca had occurred had been well advanced in the atretic process. The whole picture suggests that wherever the thecal cell persists, it possesses a peculiar sensitiveness to the trophoblastic hormone, which seems to be responsible for the lutein transformation in the theca cells.

Stromal Hemorrhage.—Certainly there would seem to be little doubt that of the three principal types of ovarian hemorrhage, the least common by far is that which occurs in the stroma directly, *i. e.*, without any relation to follicular elements or derivatives. As I have already emphasized, practically all forms of ovarian hemorrhage take their origin from the perifollicular vessels and hence are initially stromal in this narrow sense. Far less frequently ovarian hematomata are the result of the rupture of ovarian vessels into the stroma, without relation to follicular structures. Hemorrhages of this type are, perhaps, better entitled to the designation "apoplexia ovarii" than those already described. The resulting hematoma is not always easy to distinguish from the form caused by hemorrhage into an atretic follicle, as has been explained in connection with the description of the latter. In some cases, however, the distinction can be made from the irregular outlines of the stromal hemorrhage, the blood apparently forcing itself under tension along the tissue interstices (Fig. 6). That such forms of hemorrhage may occur in very young children or even in the foetus is shown in the cases reported by Riedel¹⁰ and Schultze.¹¹ In Schultze's case, a hematoma of the right ovary measuring 1½ inches in diameter was found in a child which was born dead. The thickened albuginea and the vascularity of the peritoneum demonstrated, in Schultze's opinion, that the hemorrhage was of gradual development, continuing over a period of several weeks before the death of the foetus. Riedel's case was very similar to that of Schultze.

Causes of Ovarian Hemorrhage.—No definite statement can be made as to the exciting cause of the hemorrhages which result in the formation of ovarian hematomata. It is true that many explanations have been offered for their occurrence, but in practically all cases the factors held responsible are to be looked upon as predisposing rather than exciting. These causes are, perhaps, best summarized in the following tabulation given by Stein:¹²

- | | |
|---------|---|
| Local | 1. Menstrual (excessive menstrual hyperemia). |
| | 2. Non-menstrual. |
| | (a) Active hyperemia, as acute or chronic oöphoritis. |
| | (b) Passive hyperemia, as thrombosis, torsion, varix. |
| | (c) Primary and secondary neoplasms. |
| General | 1. Diseases altering the composition of the blood. |
| | (a) Infectious diseases, as typhoid, acute exanthemata, etc. |
| | (b) General disorders of nutrition, as anemia, chlorosis, etc. |
| | (c) Hemophilia. |
| | 2. Phosphorus poisoning. |
| | 3. Burns. |
| | 4. Venous congestion of abdominal viscera, as in heart or lung disease. |
| | |

Cases illustrating the rôle of all these possible causes are to be found in the literature. I shall make no effort to review them here.

Etiological Rôle of Menstruation.—The principal point in the consideration of the etiology of these hemorrhages is the rôle played by the hyperemia of menstruation. The statement is passed on from author to author that ovarian hemorrhages are commonly due to the ovarian congestion which is said to be a part of the menstrual phenomenon. Cases have even been reported by Garrigues,¹³ Gottschalk¹⁴ and others in which large ovarian hematomata were explained as due to a species of vicarious menstruation into the ovary. This is said to occur when there is an obstacle to the exit of the menstrual blood *per vias naturales*, as after destruction of the endometrium by excessive curetting, etc. So far as I know, no proof has ever been brought forward for the correction of such views, and, indeed, no one has ever studied the problem from the viewpoint of the menstrual histories of the patients. I have, therefore, laid especial stress upon this point in the study of my own cases.

An analysis of my results yields several facts of great interest. In the first place it was noted that hematomata were most commonly found in ovaries removed at a period corresponding to the probable occurrence of ovulation, *i. e.*, from about the seventh to the sixteenth day. In practically all these cases the hemorrhage is obviously recent, or, in a few cases, it has not yet occurred but is impending. In the few cases in which hematomata are encountered in ovaries removed late in the menstrual cycle, histological examination shows that the extravasated blood is old and more or less disorganized, thus indicating again that the hemorrhage had occurred some time previously. The evidence from this group of cases, therefore, would indicate that follicular hemorrhages of the ovary, and the perifollicular congestion which precedes them, occur by predilection at or near the time of ovulation. As to the significance of these perifollicular vascular changes, I do not venture to express an opinion. That they are purely physiological, and that they are in some way called forth by the influence emanating from the "presiding ovum" of the month, would seem a natural assumption.

When we turn our attention to the time study of corpus luteum hematomata, the findings are somewhat different. The corpus luteum hemorrhages occur rather later, from about the sixteenth to the twenty-fifth day. This is exactly what we would expect if we bear in mind that most of these hematomata have their inception in the period of vascularization of the corpus luteum. As in the case of follicular hemorrhages, a careful study of the individual cases will usually serve to explain the apparent exceptions to the general rule. For example, a corpus luteum hematoma (Gyn. No. 20404) removed on the fifth day of the cycle contained old blood, and was surrounded by a broad fibrous layer within the retrogressive lutein layer. This was clearly a structure which had persisted from the preceding month and perhaps even longer. In this way, and only in this way, by careful clinical and histological correlation and by using the normal life history

as a criterion, can one interpret the various forms of ovarian hematomata which are encountered.

Effect of Hematomata upon Menstruation.—A careful analysis of the menstrual histories in the cases of this series shows that small hematomata, of whatever variety, have apparently no effect on the character of menstruation. Indeed, the only significant effect observed was in the case of the largest hematoma in the series, measuring 6 cm. in diameter. The ovary was little more than a shell, the ovarian tissue which remained at one pole showing no corpora lutea, either recent or old. The other ovary had been removed three years previously. It is, perhaps, not surprising to know that this patient had not menstruated for many months. In those cases of this series in which menstrual disorders were noted, they were practically always attributable to the coexistent pelvic disease. Certainly there is no ground for the belief held by many that the characteristic symptom of ovarian hematoma, whether of the follicular or corpus luteum type, is excessive menstruation.

Associated Pelvic Lesions.—Some of the ovaries in this group of cases would in themselves be considered relatively normal; others show extensive pathological change, such as cystic degeneration or abscess formation. In every case there was, of course, a greater or less degree of pelvic disease coexistent. By far the largest number of patients suffered with pelvic inflammatory disease. Next most frequent were the myomata; then the carcinomata, ovarian cysts and other common pelvic diseases. In other words, hematomata were, in this series of cases, found in association with practically all the usual forms of disease. Even when the removed ovaries were to all intents and purposes normal, as in some of the cases of early carcinoma of the cervix, hemorrhagic lesions of the ovary were often encountered. There can be no doubt, however, that hematomata are far more common in pathological than in normal ovaries. Martin¹⁵ found in 134 cases of ovarian hematoma that the ovaries were diseased in 88.8 per cent and normal in 11.2 per cent. Especially important as a predisposing factor would seem to be the condition commonly spoken of as cystic degeneration of the ovary, which is due to a stimulation of follicular growth and the production of an excessive number of atretic follicles.

Summary.—The present investigation was based on the study of material from 85 cases in which one or both ovaries, containing hematomata, had been removed at operation. In the overwhelming majority of cases hematomata occur in connection with the follicular structures of the ovary, although occasionally they may be the result of hemorrhage directly into the ovarian stroma. They are best classified as of the follicular, corpus luteum or stromal type.

The first-named group, *i. e.*, the follicular, comprises those due to hemorrhage into the maturing Graafian follicle and those due to bleeding into the atretic follicle. The latter form is the most frequent of all, representing the common clinical type of follicular hematoma. In the follicular type, the source of the hemorrhage is definitely traceable to the vascular ring surrounding the follicle. Such hemorrhages are primarily

perifollicular and therefore stromal, but when sufficiently great they break through into the cavity of the follicle, forming either large or small hematomata, as the case may be.

The corpus luteum hematoma is also very common, being distinguished by its yellowish wall of lutein tissue. The various clinical types of corpus luteum cysts are explainable by reference to the normal life history of the corpus luteum. The latter, like the growing Graafian follicle, may be arrested at almost any point by the occurrence of excessive bleeding into the cavity. This is especially common during the stage of vascularization, in which a moderate amount of bleeding into the corpus lumen takes place as a normal phenomenon.

Stromal hemorrhage, or "apoplexia ovarii," is not frequent, occurring most often in the course of infectious diseases, or with severe local inflammatory lesions. It has, however, been observed in the foetus and in the very young child.

A careful study of the menstrual histories of the cases on which this paper is based shows that the hemorrhage which causes follicular hematomata occurs characteristically at or near the supposed time of ovulation, *i. e.*, between the seventh and sixteenth days of the menstrual cycles. The bleeding of corpus luteum origin, as might be expected, occurs later, being apparently only an exaggeration of that normally occurring in the stage of vascularization. There is no characteristic menstrual history associated with the presence of hematomata in the ovary.

REFERENCES.

1. Novak: Abdominal Hemorrhage of Ovarian Origin. Jour. Amer. Med. Asso., 1917, LXVIII, 1160.
2. Beust (von): Lebensbedrohliche Intraabdominelle Blutungen aus Geplatzten Folliculär- und Lutein-cysten der Ovariums. Inaug. Dissert., Zurich, 1914.
3. Wolf: Ueber Haematoma Ovarii. Arch. f. Gynäk., 1907, LXXXIV.
4. Pfannenstiel: Veit's Handbuch der Gynäkologie, Bd. IV.
5. Klob: Pathologische Anatomie der Weibl. Sexual-organe. Wien, 1864 (quoted by Hedde).
6. Rollin: Des hémorrhagies de l'ovaire. Ann. de Gyn., 1889, XXXII, 354.
7. Oehman: Ueber Ovarialblutungen. Monats. f. Geburt. u. Gynäk., 1913, XXXVIII, 283.
8. Savage: On hematoma of the ovary. Brit. Gyn. Jour., 1905, XXI, 285.
9. Novak: The corpus luteum—Its life cycle and its rôle in menstrual disorders. Jour. Amer. Med. Asso., 1916, LXVII, 1285.
10. Riedel: Ein Fall von Haematoma Ovarii bei einem Neugeborenen. Inaug. Diss., Halle, 1896.
11. Schultze: Quoted by Riedel.
12. Stein: Ueber Hemorrhagien der Ovarien bei schwerer Anämie. Inaug. Diss., Halle, 1908.
13. Garrigues: Trans. Sect. on Obst. and Gyn., N. Y. Acad. of Medicine, 1889, Dec. 28.
14. Gottschalk: Zentralb. f. Gyn., 1890, XIV, 12. Deutsche Med. Wchnschr. 1896, XXII, 805.
15. Martin: Die Krankheiten der Ovarien. Bd. I.

The following additional references may be found of interest:

- Hedde: Ueber Ovarialblutungen. Inaug. Diss., Freiburg, 1913.
 Tate: Hematoma of ovary. Amer. J. Obst., 1905, LI, 653.
 Cantoni: Untersuchungen über Ovarialblutungen. Arch. f. Gynäk., 1914, CIII, 564.



FIG. 1.—Perifollicular hemorrhage in septum between two adjoining atretic follicles (*af*). Rupture into the smaller follicle is obviously impending.



FIG. 2.—Perifollicular hemorrhage (*p*) which has just broken through epithelial lining (*ep*) of atretic follicle (*af*) into its lumen.

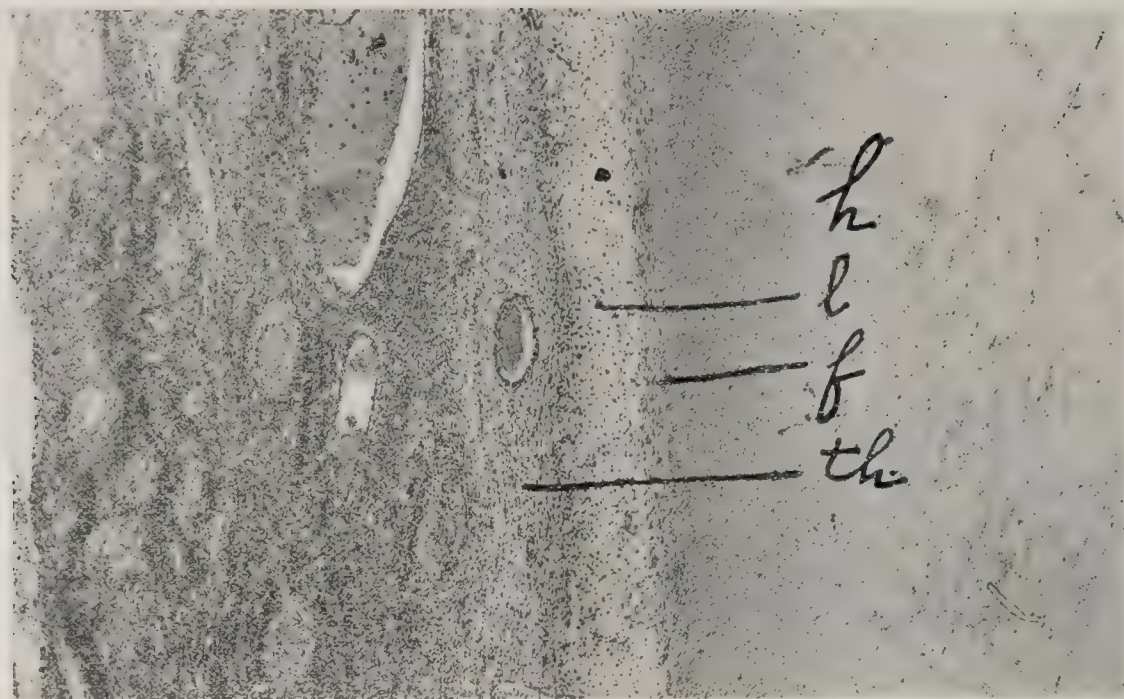


FIG. 3.—Wall of corpus luteum cyst, 5 cm. in diameter, which has apparently resulted from excessive hemorrhage during stage of vascularization. *h*—hemorrhagic contents; *f*—light layer of fibrous tissue which has developed inside the lutein layer (*l*); *th*—theca folliculi.



FIG. 4.—Wall of corpus luteum cyst, 4 cm. in diameter, in which the lutein layer has preserved its virility, and has advanced to full maturity. *l*—lutein layer; *p*—paralutein cells in theca.

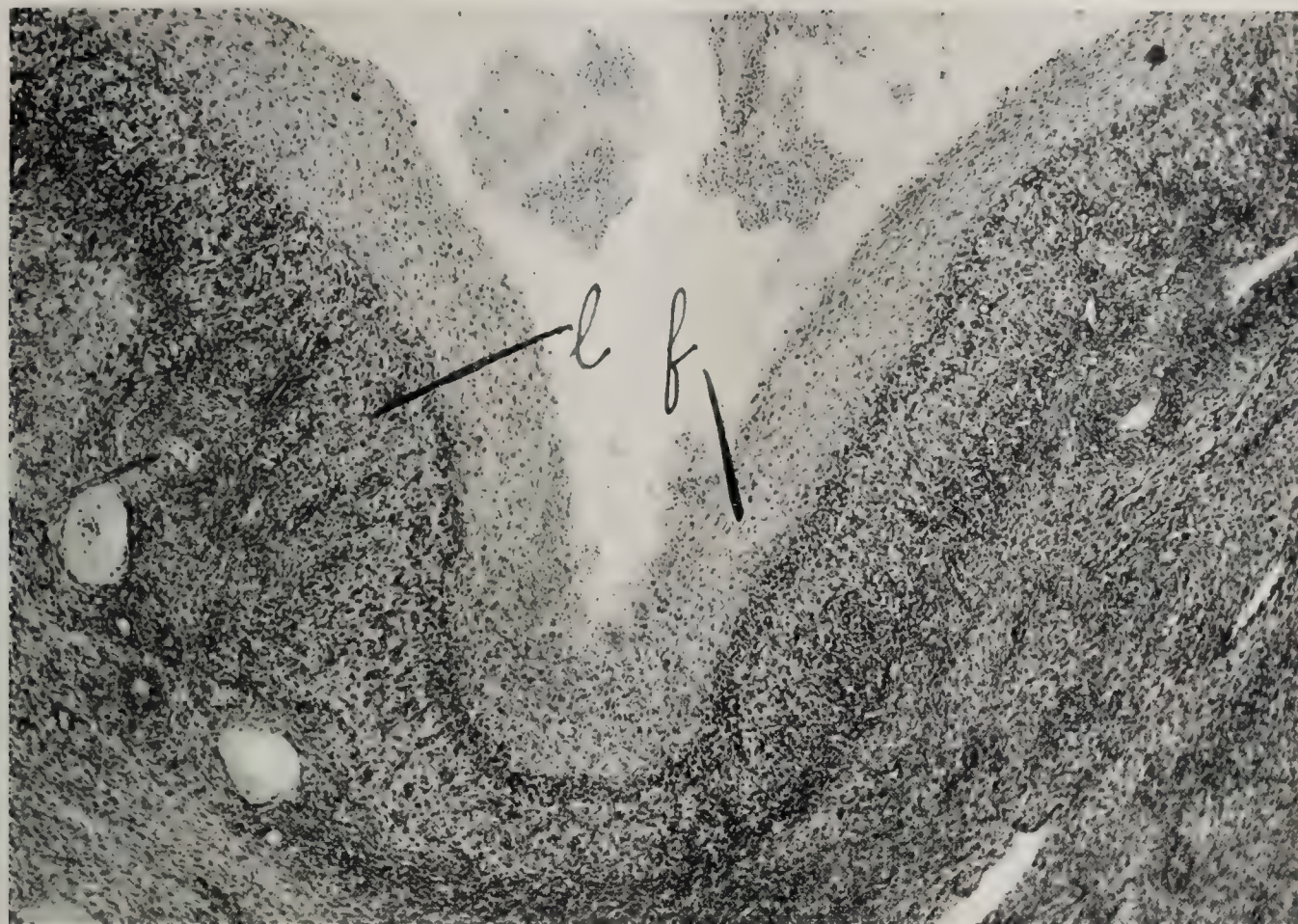


FIG. 5.—Wall of old corpus luteum cyst. Note broad zone of dense fibrous tissue (*f*) within the retrogressive lutein layer (*l*).

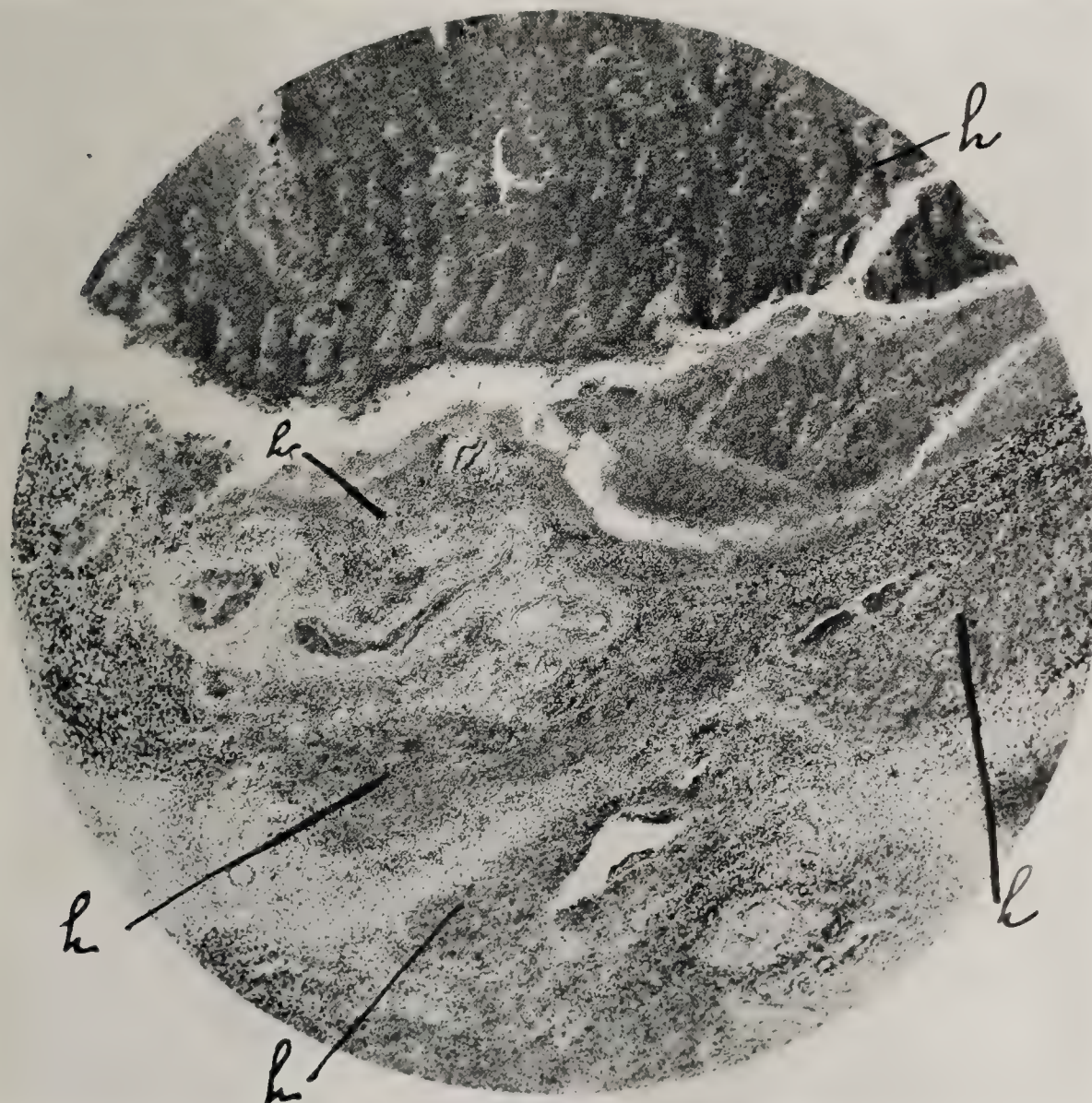


FIG. 6.—Stromal hemorrhage, with characteristic irregular outlines. Note arms of hemorrhage (*h*) projecting themselves into ovarian stroma, islands of which are left here and there.

ABSTRACTS OF PAPERS

Representing Work Done in The Johns Hopkins Hospital, but Published or to be Published Elsewhere than in the Bulletin.
Prepared by the Authors.

ON THE EFFECTS OF INJECTION OF HYPOPHYSEAL EXTRACTS (POSTERIOR LOBE AND PARS INTERMEDIA) IN THE TREATMENT OF DIABETES INSIPIDUS.*

By LEWELLYS F. BARKER, M. D., and HERMAN O. MOSENTHAL, M. D.
(From the Department of Medicine, The Johns Hopkins Hospital.)

The effects of injection of the pars intermedia and of the posterior lobe of the hypophysis cerebri in controlling the symptoms in diabetes insipidus are well illustrated by the case reported in this paper. The patient, a woman of middle age, had suffered from excessive thirst and extreme polyuria for several months. The urinary output was, at times, as much as 11 liters in the 24 hours. Work and sleep were seriously interfered with and the patient had become very nervous. The urine was of very low specific gravity, and the kidneys, as in similar cases, seemed unable to secrete a concentrated urine.

On subcutaneous administration of hypophyseal extracts (posterior lobe and pars intermedia) it was found possible completely to control both the polyuria and the polydipsia, and to raise the concentration of the urine to a normal level. Two doses of 1 c.c. each in the 24 hours were sufficient. The patient's nervousness was greatly mitigated and sleep returned. The only other effect noticeable was a movement of the bowels after each injection.

Many other forms of treatment were tried in this case but without benefit. Tethelin and adrenalin had no appreciable effect upon the polyuria.

The writers feel that their experience in this case is confirmatory of the reports of others who assert:

1. That diabetes insipidus is to be looked upon as an endocrinopathy, being due to an insufficiency of the pars intermedia of the hypophysis cerebri.

2. That the symptoms of diabetes insipidus can be controlled by a substitution therapy; namely, by the subcutaneous injection of extracts of the posterior lobe and pars intermedia of the hypophysis cerebri.

ON THE CONTROL OF DIABETES INSIPIDUS BY MEANS OF HYPOPHYSEAL EXTRACT IN A MULTIGLANDULAR ENDOCRINOPATHY (THYREO-HYPOPHYSEO-GENITAL SYNDROME).†

By LEWELLYS F. BARKER, M. D., and MARY HODGE, M. D.
Baltimore, Md.

(From the Department of Medicine, The Johns Hopkins Hospital.)

The paper includes the report of a case of multiglandular endocrinopathy with symptoms referable to the thyroid gland, the hypophysis cerebri, the inter-renal system, and the gonads.

* Paper read before the Association of American Physicians, Atlantic City, 1917. To be published in the Transactions of the Association and in the Journal of Urology.

† The full report will be published in *Endocrinology*.

Diabetes insipidus, manifested by the patient, is regarded by the writers as a hypophyseal symptom insufficiency of the pars intermedia). The polyuria and the polydipsia were controllable in this patient by subcutaneous injections of extracts of the posterior lobe (and pars intermedia). With the injections, the kidneys became able to secrete a concentrated urine. The simultaneous existence of symptoms referable to disturbances of endocrine glands other than the hypophysis did not seem to diminish the efficiency of the hypophyseal-hormone therapy.

ON A REGIMEN THAT HAS BEEN FOUND HELPFUL IN THE TREATMENT OF SOME CASES OF SO-CALLED PERNICIOUS ANÆMIA.*

By LEWELLYS F. BARKER, M. D., and THOMAS P. SPRUNT, M. D.
(From the Department of Medicine, The Johns Hopkins Hospital.)

The paper, after discussing briefly the classification of the severe anæmias, their etiology and pathogenesis, describes a regimen used by the writers in the Addison-Biermer type of pernicious anæmia which they define as a hæmolytic anæmia of as yet unknown etiology. They report that in one group of cases they have had a favorable response on applying the regimen they describe, whereas in another group of cases, indistinguishable before applying the regimen, a favorable response was not met with.

The regimen used by the writers, summarized, includes:

1. Treatment in a private room in a hospital or nursing-home.

2. Isolation and complete rest in bed under the care of a special nurse and the physicians.

3. Careful search for focal infections, and radical surgical removal of any such infections found (especially of infections of the teeth and gums).

4. Milk diet at first, followed by mixed diet rich in protein, the patient being encouraged to eat despite lack of appetite, and disregarding any consequences that may follow the ingestion of the food.

5. An abundance of fresh air, the bedroom windows being kept constantly open when the patient is inside, and the bed being run out upon an open porch in all suitable weather.

6. Dilute hydrochloric acid with and after meals on account of the gastric anacidity, followed three hours after each meal by 45 grains of pancreatin and 45 grains of calcium carbonate. If the pancreatin is not easily taken by the patient, it is omitted as one of the less important features of the treatment.

* Paper read at the American Medical Association, New York, June, 1917. To be published in the Journal of the American Medical Association, or in the Reports of the Medical Section of the Association, 1917.

7. Arsenic, usually in the form of cacodylate of soda or small doses of salvarsan, is administered as a routine. When cacodylate is given, 50 milligrams are injected intramuscularly once a day for eight days, and after an interval of two weeks a second course of eight injections is given.

8. Massage thrice weekly is given while the patient is in bed. When the hæmoglobin reaches 60 per cent, gentle exercises are begun in bed; when it reaches 80 per cent, the patient is allowed gradually to sit up and to take gentle exercise in the open air.

9. Blood transfusions are employed only in patients who on admission have a blood count below 1,000,000, or who after a trial of several weeks of the above regimen have not shown distinct improvement.

Splenectomy has not been used in the series of cases mentioned.

To the paper are appended the case summaries and blood charts of seven illustrative cases.

SOME OF THE PROBLEMS OF PLASTIC SURGERY.*

By JOHN STAIGE DAVIS, M. D., F. A. C. S.

(From the Department of Surgery, The Johns Hopkins Hospital.)

By plastic and reconstructive surgery I mean that branch of surgery which deals with the repair of defects and malformations, either congenital or acquired, and with the restoration of function and improvement of appearance.

The deformities dealt with in plastic surgery for the most part involve the skin or adjacent soft parts, rather than the bones and joints, the ligaments or tendons. The treatment of large denuded surfaces, requiring skin grafting, and of intractable wounds, should also come under the care of the plastic surgeon.

My experience has been that we seldom, if ever, find two plastic cases exactly alike, and thus no "cut and dried" methods can be employed.

The results in certain groups of cases are very slow, and in these the process is one of gradual building up. In such cases the entire series of operations should be planned with regard to the ultimate result, and not to the immediate relief of the condition.

The postoperative treatment and dressings should be done by the surgeon himself, or directly under his eye.

The simpler the operation the more likely it is to succeed, and this is especially exemplified in the operations for the relief of hare-lip.

It is wise to make haste slowly in plastic surgery, and to underdo, rather than overdo.

Thorough familiarity with the free transplantation of skin, fat, fascia, bone and cartilage is essential, as all of these tissues are constantly utilized in reconstructive work. The princi-

ples of tissue shifting, and of the use of pedunculated flaps, must be understood.

Transplantation of Skin.—The use of skin grafts is absolutely essential in plastic surgery. Skin grafts may be divided in general into *thin grafts*, where only the superficial layers are utilized and *thick grafts*, where the whole thickness or nearly the whole thickness of the skin is used. This latter division includes *small deep grafts*.

Grafts may be further classified into *auto-grafts*, where the graft is obtained from the same individual; *iso-grafts*, where the graft is obtained from another individual of the same species, and *zoö-grafts*, where the graft is obtained from a lower species.

I will not go into the technic of obtaining these grafts, but will only say that both thin and thick grafts may be successfully transplanted on healthy granulating surfaces, as well as on fresh wounds.

Iso-grafts.—I feel convinced that, when it is not possible to utilize *auto-grafts*, *iso-grafts* are well worth trying, and very good lasting results may be secured if the grafts are obtained and transplanted with the proper technic.

Zoö-grafts.—My own experience is that these grafts take readily and receive their blood supply as promptly as ordinary grafts. However, after doing well, and often when the wound is entirely healed, they will suddenly from no apparent cause begin to melt away, and will soon disappear.

Transplantation of Fat.—Free-fat-grafts are used principally for filling in depressions. They can be successfully transplanted and enough of the tissue will survive to accomplish the desired purpose. This tissue must be most carefully handled to prevent bruising. The defect into which it is placed must be perfectly dry and asepsis must be maintained.

Transplantation of Fascia.—Fascia is used in plastic surgery for a number of purposes. It is valuable for reinforcing weakened or defective tissues. New tendons may be constructed of it. It may be used alone or with fat in joints.

Transplantation of Bone and Cartilage.—Bone and cartilage are normally the supporting framework for the soft parts, and both are used for this purpose in reconstructive surgery. It must be borne in mind that free grafts of bone, either with or without periosteum, when transplanted into soft parts, will eventually be absorbed. Cartilage will live and not shrink when transplanted free, both with or without its perichondrium, into soft parts, or when in contact with bone at one or both ends.

Mucous-membrane transplantation.—Free grafts of mucous membrane are of little value when transplanted to the eyelids or into the mouth.

Subcutaneous Hydrocarbon Prosthesis.—The injection of paraffin is principally used for correcting certain deformities about the face. However, paraffin often shifts its position gradually and trickles down the tissue planes; or perhaps infiltrated tissues may thicken and cause deformities which are much worse than the original defect.

* Read before the Philadelphia Academy of Surgery, March 5, 1917.

By a *flap* we mean a mass of tissue attached at some portion of its circumference by a pedicle, which can be shifted at once or later as far as the pedicle will allow.

By a *graft* we mean a mass of tissue which is cut free to be transplanted wherever necessary.

A surface may be closed in one of four ways: First, by skin grafting; second, by sliding the edges together and suturing; third, by pedunculated flaps from tissue in the immediate neighborhood; fourth, by pedunculated flaps from distant parts. This may be done by either a single or double transfer.

In all plastic operations it is advantageous that the patient should be in the best possible physical condition, and no plastic operation should be undertaken on those with active local disease still present.

The area into which the flap or graft is to be transferred should be perfectly dry, and all hemorrhage checked.

An accurate estimate of immediate and subsequent tissue shrinkage must be planned for.

One of the most important points in plastic surgery, when tissue of any kind is transferred, is that there be no tension either on flaps or on free grafts.

The shape of the flap must correspond fairly accurately to the defect which it is to cover.

The skin of pedunculated flaps, as well as of whole thickness grafts, must be chosen with some regard to the area into which it is to be placed. The flap must be cut at least one-third larger than the area it is to fill.

The pedicle should be as broad as possible. Always aim to have the pedicle very close to the loss of substance.

As a general rule the flap should not be longer than two and a half or three times the width of the pedicle. The pedicle should not be twisted enough to interfere with the circulation of the flap.

A flap may be cut much thinner if its pedicle contains a main artery.

Twisting or too much tension on a pedicle may cause the shutting off of circulation and subsequent death of the flap.

As a rule it is best to wait for from 10 days to two weeks before amputating the pedicle of a flap.

The area from which the pedunculated flap is taken may be closed with sutures if the skin is lax, or after undercutting and sliding.

Immobilization of the part with plaster, crinolin, or splint is essential, and the dressings next to the transplanted tissue should be soft and very carefully applied.

A graft of whole thickness skin may also be placed successfully in the midst of movable scar tissue, and accomplish its purpose.

It is rare in plastic surgery that we encounter a deformity which cannot be helped by logical surgical methods.

At best we can only accomplish a certain amount, trusting in nature to complete our work.

A CASE OF PNEUMONIA OF UNUSUALLY SHORT DURATION.*

By HENRY B. CONRAD, M. D.,

Assistant Resident Pediatrician, The Johns Hopkins Hospital.

That type of pneumonia which runs its course in from one to four days is termed by Wunderlich abortive pneumonia. The comparatively recent reports of Bechtold, Krafft and Kerr have made the condition more or less familiar. Except in duration the clinical picture does not differ materially from that of pneumonia running the usual course. The majority of cases reported have shown the physical signs of pulmonary consolidation. In one of the cases reported by Krafft the pneumococcus was found in the blood, and in two it was in the sputum.

As to the pathology there are no available data since there is no mortality. The opinion is generally held that the process does not pass beyond the stage of congestion. The Roentgen-ray affords some help in solving the problem, but in using this the ignorance of what casts the shadow in pulmonary consolidation must be acknowledged.

In Case 1, D. B., the roentgenogram failed to show a shadow until the ninth day, although the symptoms of pneumonia were typical and signs of consolidation were present from the start. The question is therefore raised whether intense congestion might not give the signs of consolidation and yet cast no shadow in the roentgenogram.

The following case strongly suggests that in some cases of abortive pneumonia at least the process may go on to the stage of hepatization.

Case 2, C. D., age three years, showed the typical clinical picture of pneumonia. Defervescence was by crisis 18 hours after onset. The roentgenogram showed a triangular area of consolidation peripherally located in the upper part of the left lung. The child made an uneventful recovery and the roentgenogram four days after the crisis showed very slight remains of the consolidation.

ON THE GENESIS AND INHIBITION OF EXTENSOR RIGIDITY.†

By STANLEY COBB, ALBERT A. BAILEY and PAUL R. HOLTZ.

(From the Neurological Laboratory Henry Phipps Psychiatric Clinic, The Johns Hopkins Hospital.)

Decerebrate rigidity is a tonic contraction of those extensor muscles of the body which tend to hold the animal in a typical standing position; in Sherrington's words it is a "postural" reflex—a "Stell-reflex" according to Magnus.⁴ This rigidity only takes place when the cerebrum and thalamus have been removed, so it is supposed that the inhibitory influences which normally check this tonic extension are exerted on some "tonus centers," in the mid-brain or hind-brain, by the cere-

* Published in full in the American Journal of Diseases of Children, October, 1917.

† Published in the American Journal of Physiology, September, 1917.

brum. These normally give rise to extensor tonus, but are controlled from above by inhibitory influences, so that the rigidity shows only when that control is removed.

In this investigation we wished to gather data bearing especially on this inhibitory mechanism. Accordingly, decerebrated cats were so suspended that levers, attached to their tonically contracting extensor muscles, would record on a drum the tone changes of these muscles. The cortex of the anterior lobe of the cerebellum was stimulated electrically, and inhibition of the rigidity was recorded, preponderantly in the ipsilateral muscles. This had been previously reported by other investigators. Next the cortex was removed and the electrode was placed deeply in the subcortical structures; on stimulation here more marked inhibition was obtained, and it was more strictly ipsilateral. Finally the anterior lobe of the cerebellum was removed, exposing the dentate-rubral tracts, which on stimulation gave still more marked and more purely ipsilateral inhibition.

The inhibitory pathway has been shown by Weed to lie in the "anterior mesial" part of the internal capsule and in the "mesial fraction" of the crus cerebri (perhaps the fronto-pontine bundle or the bundle of Arnold). He also found that stimulation of this area on the cut surface of the mid-brain caused ipsilateral inhibition of the existing rigidity, an observation which we repeated on two of our cats. Moreover, Weed traced the pathway into the contralateral middle cerebellar peduncle, showing that destruction of this pontile arm stopped the inhibitory action of stimuli applied to the above-mentioned point in the crus. Further than this, he found what he considered the possible cortical representation of this tract in the superior vermis. Stimulation of this cortex caused inhibition of the rigidity, and extirpation of it caused a marked increase in rigidity. Our experiments corroborate the inhibitory effect of the cerebellar cortex. The facts (a) that we have not always obtained an increase of rigidity ipsilaterally by extirpation of the anterior part of the lobus anterior, (b) that we have found subcortical stimulation more effective than cortical, and (c) that we have found direct stimulation of the underlying superior peduncle most effective of all and most definitely ipsilateral in effect, make us believe that the inhibitory path passes down the superior peduncle.

From these observations, it seems fair tentatively to propose a pathway for the inhibitory influences which control decerebrate rigidity. Weed has traced this through the internal capsule and crus (probably as fronto-pontine bundle) to the pons, thence up the opposite middle cerebellar peduncle, and possibly to the cortex of the lobus anterior. We present evidence which indicates that the pathway leaves the cerebellum in the superior cerebellar arm (brachium conjunctivum).

If we accept this as the inhibitory path, the theory that the genesis of the extensor tonus lies in the red nuclei becomes most plausible. Weed and Brown have shown that stimulation of the cut mid-brain in the region of these nuclei causes contralateral extension of the limbs. It is in the red nucleus

that the inhibiting path seems to end. Therefore we may reason that normally the red nuclei give rise to tonic impulses causing an extensor posture, that these are controlled from above by inhibition along the pathway described, and that cutting this pathway allows over-activity of the nuclei and hence decerebrate rigidity.

In order exactly to determine the relation of the red nuclei to decerebrate rigidity, other experiments were carried out. Cats were prepared as above described, and their brain-stems were transected at levels both above and below and through the red nuclei. Notes on the duration and character of the resulting phenomena were made, and these were compared with the anatomical findings in serial sections of the brain-stem.

A comparison of the results of 18 preparations cut at various levels show a difference in character between the typical decerebrate rigidity of the mid-brain preparation, and the variable tonic extension of the hind-brain. When the red nuclei are present there is a steady rigidity. This rigidity can be inhibited by stimulating any point on the inhibitory pathway, and this path largely ends in the red nucleus. Therefore, it seems, a large part of the activity arises in the red nuclei; probably a reflex activity set up by the direct cerebellar tracts. When we cut further back so as to destroy this reflex arc, the tonic extension becomes less, but is still elicited by increasing the quantity of afferent stimuli. Even in cord lesions some types of rigid extension appear, and Magnus in a recent paper contrasts the postural reflexes of "pons animals" with those found in animals with the mid-brain intact. From the ontogenetic point of view Weed's paper on "The Reactions of Kittens after Decerebration" brings in more evidence to show that we are dealing with a complicated mechanism, the activities of which are graded according to the level of integration of the animal as well as the level transection of the neural axis. It is hoped that further investigation will throw some light on a subject the practical application of which is so great in relation to such problems as clonus, contracture, muscle tonus, and body posture.

CONCLUSIONS.

1. Stimulation of the superior cerebellar arm in decerebrate cats causes ipsilateral inhibition of their rigidity.
2. The inhibition of decerebrate rigidity by stimulation of the cortex of the anterior lobe of the cerebellum appears to depend on stimulation of the underlying superior cerebellar arm.
3. A kind of extensor rigidity (not the typical "decerebrate rigidity" of Sherrington) is found in preparations transected below the red nucleus. This extensor tonus is lost when the transection injures the vestibular nuclei.
4. Stimulation of the superior cerebellar arm elicits no inhibition of extensor tonus when the red nuclei are not left in the preparation, or when the dentate-rubral path is cut.

SOME EXPERIENCES IN THE GERMAN RED CROSS.*

By CLARENCE A. NEYMANN,

Assistant in Psychiatry, The Johns Hopkins Hospital.

After a description of the conditions which led up to a systematized treatment of mental cases in the German Army, the various types seen in the base hospitals are portrayed. The psychoneuroses fell into three main groups.

One of these groups stood out before all others and was of course immediately labeled. It was called "Granatfieber," grenade fever. These individuals, at least those that came under my observation, were usually stoop-shouldered and narrow-chested. They had a poor physical build and a naturally weak constitution. All complained of indigestion (the hospital served good though rather coarse food), backaches and headaches. However, they fell in with the routine pretty well and only showed symptoms when the experiences at the front were dwelt upon. Then, especially when grenades were mentioned, they immediately grew pale, trembled, and in some cases so far lost control of their legs that they fell down. After such an experience they were restless and nervous and could not sleep without hypnotics for a number of days. This reaction was not necessarily dependent upon the question of their return to the front, but could be brought about by a mere casual mention of explosions, grenades, shells, mines, etc.

A second class that was fairly distinct consisted of those individuals who had had especially trying experiences and

then simulated some internal or mental disorder, for which men in their company had been sent to the rear. This simulation often persisted for months even after they were told that they were unfit for duty in the field. One of my patients had attacks of pseudo-epilepsy so manifestly genuine that the reacting pupils during the attack and the account of events immediately preceding the first attack were the only things that clinched the diagnosis.

From this to mere slackerdom, which we may possibly consider as a third group, is but a step and one sees all intermediate stages. It is hardly to be wondered at that a man who naturally has not much strength of character grows tired after months of trench life and quits, either by exposing himself or by simulating some disorder.

Quite opposite from the reaction of these naturally weak and neurotic individuals is that of those slightly mentally deficient. The troops from Bavaria are notably brave and yet among their wounded one finds many high-grade morons. Such individuals usually make good soldiers.

Besides these main types of mental disturbances all sorts of individual reactions were observed. Patients who had gone through depressions in previous years again became depressed. Hypo-manic individuals became very wild and lost almost the last remnants of civilization. Just after the return from the front the behavior of this last class was such that they were exceedingly difficult to control and constantly broke the hospital routine. All these facts agree with our modern psychiatric view of the specific reaction of each individual.

* The Journal of Mental Hygiene, July, 1917.

NOTES ON NEW BOOKS.

A Manual of Pharmacology, and its Applications to Therapeutics and Toxicology. By TORALD SOLLMANN, M. D. Cloth, \$4.50. (Philadelphia and London: W. B. Saunders Co., 1917.)

A Laboratory Guide in Pharmacology. By TORALD SOLLMANN, M. D. Cloth, \$2.50. (Philadelphia and London: W. B. Saunders Co., 1917.)

These two books are intended to take the place of the author's well known manual of Pharmacology which formerly included both. In revising the work, the matter had to be so expanded that two volumes were deemed necessary, one devoted to pharmacology proper and the other to directions for laboratory experiments. It is the ambition of the book, as the author states in the preface, to make it serve both as a text-book and a reference book. A single book which undertakes to fulfill both of these requirements is almost certain to emphasize one at the expense of the other, and the present work is no exception to this rule. Although an attempt is made to differentiate between the more important and less important pharmacological effects by arranging the text in different types, on the whole the Manual of Pharmacology would seem to be more suitable for advanced students and the specialist in pharmacology, rather than for the beginner. Aside from this criticism, the present work is probably the most comprehensive reference handbook on pharmacology in English.

The Manual contains much matter which is not generally included in the ordinary text-book. Thus, in the first part, a great deal of valuable pharmaceutical information is given. Prescription writing, metrology, posology and even coloring and flavoring

reagents receive a considerable amount of attention. There are very interesting general remarks on the Treatment of Disease, Chemical Basis of Pharmacology, General Principles of Toxicology and the more important facts concerning Physical Chemistry.

Although the author, as a zealous member of the Council on Pharmacy and Chemistry of the American Medical Association has perhaps unnecessarily curtailed his discussion of certain classes of drugs which have been greatly abused by the profession, such as the antipyretics, most of the more important pharmacological groups of drugs receive adequate consideration. The treatment of Anesthetics and the discussion of the Theories of Narcosis are especially good, and no less so the descriptions of the Atropin group, of Strychnine and of the Ergot alkaloids. A great many newer remedies and reagents are noted, such as the more recent organic Arsenicals, Optochin, and various organic preparations. There is also an interesting though brief description of Radium and other radioactive substances and of colloid metals. Although the Manual, like all text-books, is some five years behind the times, there is certainly an attempt made to include the references to all of the most important recent work in pharmacology. The literary index at the end, while not complete, will be found very convenient by the investigator as a starting point for tracing out the literature on the more important subjects.

The Laboratory Guide, like the Manual, describes a great many experiments, for instance, vividiffusion, which can be performed only by the specialist. All the ordinary pharmacological experiments, however, are fully given, making it convenient for teaching purposes. The first part is devoted mainly to chemical experi-

ments and pharmacognosi; the second part deals with more purely pharmacological experiments. A list of dosages for animals is appended. On the whole, the Manual of Pharmacology and the Laboratory Guide Book will be found very useful handbooks by every pharmacologist and should be on the reference shelf of every laboratory.

D. I. M.

Cardio-Vascular Diseases. By DR. THOMAS E. SATTERTHWAITE. (New York: Lemcke and Buechner, 1912.)

In a subject in which there has been so steady and so definite advance as has taken place in cardio-vascular study, it is difficult to review fairly a book written five years ago. In Dr. Satterthwaite's book, which represented the book-form presentation of a collected series of his monographs up to 1912, one is, of necessity, struck by omissions, which are interesting in the fact that one thereby comprehends the advances made in the understanding of cardiac activity—especially since the author states that he has tried to limit himself to the description of those "newer" features of the subject that have a definite bearing on diagnosis and treatment.

The illustrations are not distinctive and are in no small part cuts of different instruments that would obtain in an outfitter's catalogue. The electrocardiograms are poorly reproduced and are characterized somewhat by splintering. The text represents a few general lectures to post-graduates who have been out of touch with university opportunities and who are particularly interested in treatment. Many of these would probably be attracted by the use of the high frequency current and carbon dioxide, rather than by the more practical but less impressive therapy resulting from a quiet study of the patient's life, with a readjustment of the relationship between rest and activity to the end that the demands on the heart may be less than it can supply.

E. W. B.

Studies in Blood-Pressure—Physiological and Clinical. By GEORGE OLIVER. Third edition. Cloth, \$3.00. (New York: Paul B. Hoeber, 1916.)

The death of Dr. George Oliver, at Christmas time, 1915, was a sad loss to the many friends in his native land and the privileged few on this side the Atlantic who had been permitted to pass beyond the appreciation of his published work to the knowledge of one of the most lovable of English gentlemen. To be numbered among the latter was the good fortune of the reviewer, who welcomes this opportunity to record his admiration for the earliest and foremost English-speaking student of blood-pressure, and his affection for a nature overflowing with kindness and goodwill. He combined thorough physiological training with ripe clinical experience, and his writings reflect the intimate blending of the two. Constant interest in the underlying mechanisms and their elucidation, balanced by practical wisdom, makes this last edition of his book of unusual value to every physician who wishes to base his treatment of hypertensive patients on sound theory and sane clinical observation.

The first edition of Dr. Oliver's "Studies in Blood-Pressure," published in 1901, blazed a narrow trail into the then unexplored domain of clinical sphygmomanometry. The second, in 1908, much enlarged and rewritten, recorded the great progress ahead made. At the time of his death he had fortunately almost completed a third rewriting, which contained all the important additions to knowledge and method which had accrued in the interval. Happily his friend, Professor Halliburton, at once took charge of the publication of this third edition, which appeared last summer.

The book is admirably suited to the needs of the practitioner. It contains all the essential bibliographic references, but no others, and has none of the features of a compilation. It is primarily the straightforward exposition of existing physiological and clinical

knowledge of human blood-pressure and its disorders by one who sought always to improve his own methods of diagnosis and treatment. The chapters on fundamental data are quite free from that pseudo-physiology, which is so harmful to the mind that falls under its spell. The chapters dealing with method are absolutely clear and set forth all the sources of fallacy in clinical measurements, whether oscillatory or auditory, and how they may be avoided. The treatment outlined is conservative, but real. Dr. Oliver treated large numbers of hypertensives during his years of practice at Harrowgate and knew how much he could help them, as well as how to avoid doing them harm. The concluding chapters on arteriometry and on venous and capillary pressures show the breadth of his interest in the relation of all the elements of the peripheral vascular mechanism to the maintenance of a normal circulation. It is to be hoped that English-speaking physicians generally will avail themselves of the knowledge Dr. Oliver has made so accessible for their guidance in caring for one of the most important groups of their patients.

T. C. J.

Pharmacology and Therapeutics. By HORATIO C. WOOD, JR. Second edition. Cloth, \$4.00. (Philadelphia: J. B. Lippincott Co., 1916.)

The new edition of this work makes it a thoroughly complete text-book of present day drugs and their practical application. The pharmacology is carefully brought up to date and concisely and pleasingly presented. Therapeutics are limited to the Action of Drugs almost entirely. The volume does not attempt to deal with the many general and special therapeutic problems outside the realm of drug treatment, but such a limitation of scope is necessary in a book of its size. The discussion of the use of drugs in disease is, however, essentially practical, complete and full of sound clinical advice.

One must take issue with the statement on p. 226 that Addison's Disease of the adrenal glands is "usually cancerous" in nature. The classification of the Anæmias seems rather to sacrifice accuracy to brevity. They are divided into Accidental Anæmia, in which there is said to be an equal reduction of hæmoglobin and red blood cells; Chlorosis, in which there is a relatively greater reduction of hæmoglobin; and Pernicious Anæmia, in which the red cells especially are reduced. If one accepts this classification, he is forced to include under the diagnosis of Chlorosis many cases of secondary anæmia of varied origin, which bear no relation to Chlorosis as a clinical entity.

Dr. Wood's book is as complete, scientific and practical presentation of the action and use of drugs as could be contained in a single volume of 455 pages.

J. T. K., JR.

Materia Medica for Nurses. By A. S. BLUMGARTEN, M. D. Second edition. Cloth, \$2.50. (New York: Macmillan Co., 1916.)

This is much like other books of a similar nature—a condensed summary of an important subject. In fact, it is so concentrated as to be more like a dictionary than a text-book. For hasty reference to preparations and dosage of drugs it would be very useful and probably is as good a book as one could get to cover a large subject in a few words. For a nurse of investigating mind it would prove inadequate, yet one can find very quickly the salient facts about Materia Medica.

The author speaks of a Cardiac Stimulant as a drug which "makes the heart beat stronger and faster." This is rather too dogmatic, as our common cardiac stimulants, digitalis and strophanthus, decrease the rate of the heart and the nurse should know it. The same quotation illustrates the rather frequent use of the adjective for the adverb where the latter is clearly intended.

On the whole, the work is accurate and is a good handbook for a nurse at work.

J. T. K., JR.

Report of the First Expedition to South America—1913. Harvard School of Medicine. (Cambridge: Harvard University Press, 1915.)

This volume is a model of its kind. The subjects dealt with at greatest length in the report are Verruga Peruviana and Oroya Fever. These conditions, formerly believed to be different manifestations of the same disease, the authors have definitely separated into distinct clinical entities. Case histories, detailed records of clinical investigations, pathological reports, animal experimentation and some entomological study are all carefully given. As the result of this work it has been shown that Oroya Fever—a disease associated with fever and intense anæmia, and having a high death-rate—is caused by a microorganism, previously described by Barton and called *Bartonella bacilliformis*. This protozoon is a parasitic invader of the red blood cells and of the endothelial cells. All attempts at animal inoculation yielded negative results. Although not definitely proven, an arthropod is believed to be the intermediate host.

Verruga Peruviana—a disease with some fever and slight anæmia—is characterized by definite skin eruptions. No microorganisms have been discovered, but animal experiments, especially with monkeys, have yielded beautifully positive results. A filtrable virus is supposed to be the etiological factor, but so far this has not been definitely proven.

The finding of both diseases in the same individual and the further obscuring of the pictures by the prevalent malarial infections and by paratyphoid have all been largely responsible for the confusion concerning these two conditions.

The work also contains a short consideration of the clinical picture, pathology and etiology of Uta—an ulcerative inflammatory skin infection—prevalent in Peru. A species of *Leishmania* is shown to be the etiological factor in its production.

There is also an account of the negative results from efforts to confirm Seidelin's findings in the red blood cells in cases of yellow fever. Another interesting article is that on various flies and mosquitoes brought back from the trip. A new linguatulid found in crocodiles in Ecuador is also described.

The splendid illustrations throughout the book are a valuable addition to the text. M. D. B.

The Diagnosis and Treatment of Abnormalities of Myocardial Function. By T. STUART HART. (New York: The Rebman Co., 1917.)

It is a pleasure to review so interesting a book as has recently been presented by Professor Hart of Columbia. Abnormal Myocardial Function is a successful attempt to give physicians and students the present status of cardiac physiology—both normal and pathological—especially as obtained by the newer methods of study. It exemplifies the clinical application of the laboratory in this particular field. Illustrations are plentiful and, pleasantly enough, they are practically all original. The electrocardiograms are excellent and are, all in all, among the best reproduced both for their text application and their technical appearance. Although there may be conclusions to some of Professor Hart's deductions and although occasional statements are possibly too dogmatic, in view of the existing evidence, the book is unquestionably one of the best in its field, theoretical possibilities being balanced by good hard sense. The references are good and represent a thorough familiarity with the literature. E. W. B.

The New Method in Diabetes. By J. H. KELLOGG, M. D. (Battle Creek, Mich. Good Health Publishing Co., 1917.)

This small book represents an effort at a complete summary of our knowledge of diabetes in a very few pages. Under these circumstances, the logical sequence of the text is necessarily halting, and it is difficult for the reader to follow the flow of thought, unless

he is well acquainted with the subject. The mode of treatment advocated by Dr. Kellogg, a low meat dietary with a disproportionate amount of fat, especially in cream, and a considerable quantity of starch in vegetables, is somewhat contrary to the usual treatment accepted as a standard one to-day. However, it seems to have yielded results in the hands of Dr. Kellogg, and the recipes furnished may be of definite aid to those who wish to follow his lead. M. D. B.

Practical Therapeutics. By H. A. HARE. Sixteenth edition. Cloth, \$4.75. (Philadelphia and New York: Lea & Febiger, 1916.)

As in preceding editions, this book is divided into four parts. The first, entitled "General Therapeutic Considerations," gives the usual introductory information regarding weights and measures, prescription writing, drug incompatibilities, etc. In the second, headed "Drugs," is found a list of the medical therapeutic agents, including those listed in the new U. S. P. and the New B. P. There is given a short account of the physiological action of each drug together with its therapeutic use and the results of overdosage. Under "Remedial Measures other than Drugs" and "Feeding the Sick," the heading of the third part, are described procedures varying from all forms of hydrotherapy and thermotherapy to serum treatment, transfusions, kataphoresis, acupuncture and the preparation of food for the sick. "The Treatment of Disease" is discussed in the last part. G. E. de Schweinitz has contributed the articles on diseases of the eye; B. C. Hirst, those of the puerperal state; E. Martin has written on antiseptics, gonorrhea and syphilis. Practically all the common disorders are discussed, including even such things as the medical handling of anal fistula and alcohol injections for trigeminal neuralgia.

With its alphabetical arrangement of subject matter, the book is well planned for ready reference. The combined collection of scientific and empiric information gives the work, however, a pseudo-scientific coloring. To have emphasis laid on the cure of lumbago by the insertion of sterile needles into the back muscles and to read that malaria is "practically always the result of a mosquito bite" is rather startling information to be given in a scientific work of to-day. The directions for alcohol nerve injections make the procedure sound so simple as to incur the danger of enticing those totally unskilled for such a procedure into an attempt. The formula for Dakin's solution also sounds very easy, whereas in reality the knowledge of a good chemist is needed.

If perhaps the scope of the book had been less broad and the consideration of the various topics a little more deep and, in some cases, more accurate, the results would have been more acceptable to the truly scientific medical man. M. D. B.

The Growth of Medicine. By ALBERT H. BUCK, M. D. Cloth, \$5.00. (New Haven: Yale University Press, 1917.)

Most of our information we take on faith, believing as facts most of the data that are transmitted to us because they are generally accepted or else come burdened with the overpowering weight of authority. The common facts that rule our lives and guide our daily prudence we clothe with an absolute truthfulness, building the universe upon their necessary existence. Only the recondite philosopher is interested in the nebulous antiquity of the mind when first it groped to consciousness and welded these simple but powerful mental tools from the dim memories of ages of struggle. The discoveries of later years, and especially the novelties of modern science, arouse our profound interest and astonishment, but wonder nearly always exceeds curiosity and complacency usually throttles both. We must, of course, accept most of our knowledge upon such simple faith; we could not, if we would, investigate the foundation of it all. However, there is always a small part of human knowledge and experience in which we daily work and live, and of this small part we must know the

facts, if we are fully to appreciate its present problems. A truth is never so appealing as when we are familiar with the slow steps of progress upon which it has been built. We never wholly grasp its force unless we know the underlying data from which it is derived and the methods that have borne it birth. From this broad perspective we see principles of practice in their true light, not as final, settled opinions but as a shifting platform of human endeavor gained after ages of struggle from which man reaches out eagerly and hungrily for new adventures and conquests.

To have this perspective is to know the history of the phase of human endeavor that engages our attention. We physicians are notoriously insensible to the rich and inspiring past of our art. The age is so full of absorbing discoveries, and the demands of practice are so exacting that there is not enough for ordinary zeal and interest to keep abreast with the advances of the day. Nevertheless to be imbued with the spirit of this advance, to taste the real flavor of progress, we must have a thought for the tillers who prepared the soil for our rich harvest, an appreciation of their labors, with a knowledge of the difficulties they encountered and of the rude instruments with which they overcame them. Dr. Buck's book will prove to many a solution of the conflicting demands of practice and scholarship. In brief compass and in entertaining style he sketches the history of medicine. Every physician can get information and pleasure from reading it. No doubt it will prove a stimulus to interest in the history of medicine among the profession of America, and it is to be hoped that it may arouse a chosen few diligently and intensively to cultivate this neglected corner of our art.

L. H.

The Development of the Human Body. A Manual of Human Embryology. By J. PLAYFAIR McMURRICH, A. M. Fifth edition. Cloth, \$2.50. (Philadelphia: P. Blakiston's Son & Co., 1915.)

The fifth edition of this popular manual of human embryology is even more compact than its predecessors and, like them, reflects the careful work of the author in bringing the contents up to date. The well known merits of this volume, which have been dealt with in reviews of the earlier editions, do not need reiteration here, and attention will be directed principally to the evidences of revision. Among these may briefly be mentioned the section on spermatogenesis (p. 13) which has been largely rewritten, and includes a reference to the latest investigations upon the accessory chromosomes. It is of interest to note that the spermatogonia which are destined to become Sertoli cells are characterized by containing a curious rod-like crystalloid—the anlage, apparently, of the crystalloids of the mature sustentacular cells; also that the spiral filament of the spermatozoön is now regarded as having

been developed from the "cytoplasmic plastosomes" instead of merely from the "cytoplasm," as in the last edition. Indeed the recent interest manifested in cytoplasmic bodies in general, in their relation to cell differentiation, is represented in the sentence which the author devotes to the mitochondria (p. 4). The former description of the origin of the sex cells has been modified to include the views of Fuss (p. 346), who derives these elements in the human subject from the endoderm of the digestive tract.

On page 25 the more recent views as to the function of the corpus luteum verum are set forth; here also Bischoff's theory of the origin of the lutein cells from the granulosa cells is considered to be well established rather than an open question, as heretofore. A new paragraph, illustrated by a diagram, is added, containing the results of recent work on the pronephric system (p. 336).

The wide field of human embryology is covered in an astonishingly comprehensive manner considering the small compass of the book, but, on account of the limitation in space, an exhaustive discussion of all points has not been possible. Thus only one of the several hypotheses dealing with the metamorphosis of the red blood-corpuscle—that which postulates an extrusion of the nucleus apparently *en masse*—is presented (p. 223).

To designate the differentiation of certain cells of the dermis into fat cells the pathological term "fatty degeneration" is used (p. 141). Again, the basophile cells of Ehrlich (p. 225) are regarded as leucocytes in process of degeneration—a view with which not all hematologists will agree. It should be mentioned here that the terms "polymorphonuclear" and "polynuclear" which the author links with the basophile leucocyte are usually applied to the neutrophile.

The epiphyseal cartilage (p. 154) is said to be transformed into bone on both its surfaces, and although this is strictly true, yet the growth is so much greater on the diaphyseal side that some authors (Macewen) prefer to speak of the "diaphyseal cartilage."

The text is splendidly illustrated, the figures being abundant, well chosen and frequently original. It is, indeed, difficult to see how the volume could be improved in this respect unless, perhaps, a good diagram, giving a view from the front, were added to assist in the description, on page 325, of the complicated attachment of the mesentery to the dorsal abdominal wall.

On the whole it can be said without a doubt that the work is easily the best in its field, and the fact that it is now in its fifth edition (the advent of which is only two years removed from that of the fourth) speaks eloquently for the high esteem in which it is held by the profession and student body of biologists in general and medical biologists in particular. It is safe to say that this issue will enjoy an even fuller measure of prestige than any of its forerunners.

C. C. M.

BOOKS RECEIVED.

Elements of Anatomy and Physiology for Nurses. By Percy M. Dawson, M. D. 1917. 12°. 279 pages. Macmillan Company, New York.

Association of American Physicians. Transactions. Volume XXXI. 1916. 8°. 515 pages. Printed for the Association, Philadelphia.

The Breast: its Anomalies, its Diseases, and Their Treatment. By John B. Deaver, M. D., LL. D., Sc. D., and Joseph McFarland, M. D., Sc. D. Assisted by J. Leon Herman, B. S., M. D. With 8 colored plates and 277 illustrations in text. 1917. 4°. 724 pages. P. Blakiston's Son & Co., Philadelphia.

Cataract, Senile, Traumatic and Congenital. By W. A. Fisher, M. D. 1917. 8°. 119 pages. Published by Chicago Eye, Ear, Nose and Throat College, Chicago.

New York Obstetrical Society. Transactions. Volume for 1911-1913; volume for 1913-1916. Edited by George W. Kosmak, M. D. Reprinted from the *American Journal of Obstetrics*. 8°. William Wood & Company, New York.

Studies on Aerobic Spore-Bearing Non-Pathogenic Bacteria. From the Laboratory of Hygiene and Bacteriology, Johns Hopkins University. By W. W. Ford, C. A. Laubach, J. S. Lawrence, J. L. Rice. 1916. 8°. 533 pages.

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THE CULTIVATION OF TUBERCLE BACILLI FROM THE CIRCULATING BLOOD IN MILIARY TUBERCULOSIS.*

By MILDRED C. CLOUGH, M. D.

(From the Medical Clinic of The Johns Hopkins Hospital.)

The occurrence of tubercle bacilli in the circulating blood in miliary tuberculosis has been recognized for a long time. The pathological anatomy of this disease indicates that tubercle bacilli must be distributed throughout the body from a primary focus by way of the blood stream. Even before the discovery of the tubercle bacillus, Villemin in 1868, and later others, produced tuberculosis in animals by inoculation with blood, first from experimentally infected animals, and later from tuberculous patients. Since that time, the presence of tubercle bacilli in the circulating blood of tuberculous patients has been proven by many investigators by the production of generalized tuberculosis in guinea-pigs inoculated with blood. The results obtained by a number of different authors are summarized in Table I.

As is shown in the table, there is a great discrepancy in the percentage of positive results obtained by different authors from the inoculation of guinea-pigs with blood. This may be explained in two ways.

First, in some cases, the diagnosis of tuberculosis in the inoculated guinea-pigs is unreliable. For example, in the series reported by Liebermeister many of the guinea-pigs reported as tuberculous died in from one to three weeks (or even less) after inoculation, obviously of an acute intercurrent infection, without distinctively tuberculous lesions. No histological studies were reported, and the diagnosis was based

on staining acid-fast rods in smears from the bloody peritoneal exudate or from the organs. Some authors, for instance Kennerknecht, considered a guinea-pig tuberculous in the absence of gross lesions or histological changes if they found acid-fast bacilli in the blood of the animal, or even in the sediment from the organs when digested with antiformin. Sturm even went so far as to call a guinea-pig tuberculous because he was able to find Gram-positive bacilli and Much granules in the sediment of the digested organs. In other reports, including those of Haga, Klemperer, and C. Fraenkel, the character of the lesions found in the inoculated animals is not described, and it is impossible to draw any conclusions as to the reliability of the results.

Secondly, the type of cases studied differs in the different reports, some authors including only miliary tuberculosis in their statistics, and others only pulmonary or other types of tuberculosis. In this table the cases of miliary tuberculosis reported are separated from tuberculosis of other types, and included under a different heading.

In all, I have collected from the literature 1508 cases of tuberculosis studied by guinea-pig inoculation, of which 195 gave positive results. The percentage of positive results (12.9 per cent) in this series corresponds approximately to that obtained by Fischer in a compilation of 1250 cases with 17 per cent positive inoculations, by Fraenkel of 500 cases with 20 per cent positive results, and by Austrian and Hamman of 863 cases with 11 per cent positive inoculations. My figures are undoubtedly too high, because included in my table are

* This work was done under the Mary Putnam Jacobi Fellowship of The Woman's Medical Association of New York City.

TABLE I.—GUINEA-PIG INOCULATIONS WITH BLOOD FROM TUBERCULOUS PATIENTS.

Name.	Date.	Total cases.	No. +.	% +.	No. of military cases.	No. +.	% +.	Ante or post mortem.	Amount of blood injected.	Type of tuberculous lesion produced.	Remarks.
Meisel.....	1884	8	8	100	8	8	100	1 A. M. 7 P. M.	Small amt. of clot.	Gross lesions.	
Kühnau.....	1897	12	1	8	4	1	25	A. M.	Not stated.	
Jousset.....	1903	6	2	33	0	0	0	A. M.		
Bergeron.....	1904	26	1	4	2	1	50	A. M.	5-10 c.c.		
Gary.....	1905	16	5	31	1	1	100	A. M.	All gross lesions.	
Lüdke.....	1906	14	5	35	2	2	100	A. M.	5-10 c.c.	Gross lesions. Tubercle bacilli stained in organs.	3 positive cases in advanced pulmonary tuberculosis.
Huguenin.....	1908	1	1	100	0	0	0	P. M.		Blood of a fœtus.
Anderson.....	1909	48	0	0	0	0	0	A. M.	2½ c.c.		47 pulmonary cases with bacilli in sputum. One joint case. Parallel cultures negative.
Dailey.....	1909	17	0	0	2	0	0	A. M.	1-2 c.c.		
Liebermeister.....	1909	50	20 (?)	40	0	0	0	A. M.	3-6 c.c.	Questionable gross lesions. Diagnosis in many cases depends on staining bacilli in peritoneal exudate.	Pulmonary cases.
Sturm.....	1911	50	23 (?)	46	0	0	0	A. M.	5 c.c.	Gross lesions in a few cases. Many results based on staining bacilli in sediment of digested organs. 3 cases seem certainly, and 4 probably positive.	
Fraenkel, C.....	1912	50	7	14	0	0	0	A. M.		Pulmonary cases.
Bacmeister and Reuben	1912	15	0	0	0	0	0	A. M.		Incipient pulmonary cases.
Kennerknecht....	1912	13	13 (?)	100	0	0	0	A. M.	Not given.	Some gross lesions. Diagnosis mainly depended on staining bacilli in blood or organs of guinea-pigs.	
Liebermeister.....	1912	50	20 (?)	40	0	0	0	A. M.	3-6 c.c.	No protocols.	Reports 100 cases with 40 positive results, including 50 already listed (1909).
Nobécourt and Darré	1912	40	4	10	2	2	100	10-20 c.c. in 2-3 pigs.		1 case tuberculous meningitis +. 1 case acute tuberculous bronchopneumonia +.
Rumpf.....	1912	35	3	9	0	0	0	A. M.	Not given.	Not stated.	
de Amicis.....	1913	30	0	0	0	0	0	A. M.	5-9 c.c.		Tuberculosis of lungs, glands, peritoneum, pleura, kidneys.
Bacmeister.....	1913	15	4	27	0	0	0	A. M.	10 c.c.	Gross lesions and stained smears.	4 positive only after a tuberculin reaction.
Bernard et al.....	1913	2	2	100	2	2	100		
Bogasau.....	1913	41	0	0	0	0	0	A. M.	Not stated.		"Phthisis" cases.
Dreesen.....	1913	36	1	3	0	0	0	A. M.		Also 30 normals—all negative. Positive case, advanced phthisis.
Elsässer.....	1913	25	0	0	0	0	0	A. M.		All pulmonary cases.
Fraenkel, E.....	1913	24	2	8	0	0	0	A. M.	Not stated.	Gross lesions and stained smears.	All pulmonary cases.
Haga.....	1913	81	24	30	0	0	0	A. M.	1-2.5 c.c. in 4 pigs.	Not stated.	
Kachel.....	1913	26	4	15	0	0	0	A. M.	4-5 c.c.	Gross lesions not extensive.	One other pig gave a + tuberculin reaction.

TABLE I.—GUINEA-PIG INOCULATIONS WITH BLOOD FROM TUBERCULOUS PATIENTS.—(CONTINUED).

Name.	Date.	Total cases.	No. +.	% +.	No. of miliary cases.	No. +.	% +.	Ante or post mortem.	Amount of blood injected.	Type of tuberculous lesion produced.	Remarks.
Lange and Lindemann.	1913	78	1	1	0	0	0	A. M.	Not stated.	Animal experiments not completed.
Mayer.....	1913	25	0	0	1	0	0	A. M.	Not stated.	24 pulmonary cases.
Querner.....	1913	37	0	0	0	0	0	A. M.	10 c.c.	All pulmonary.
Rist et al.....	1913	50	0	0	
Rothacker and Charon.	1913	46	1	2	1	1	100	A. M.	3 c.c.	Gross lesions.	Several advanced pulmonary cases.
de Verbizier.....	1913	15	0	0	0	0	0	A. M.	Sediment of 5 c.c.	
Baetge.....	1914	29	8	27	0	0	0	A. M.	6 c.c. each in 2 pigs.	Not stated.	28 pulmonary, 1 meningitis negative. Only 1 of each pair of pigs died.
Fischer.....	1914	13	0	0	2	0	0	A. M.	1-4 c.c.	2 miliary cases probably chiefly meningeal.
Haas.....	1914	24	0	0	0	0	0	A. M.	6-7 c.c.	Surgical cases.
Klemperer.....	1914	25	6	24	2	2	100	A. M.	5 c.c.	Not stated.	16 pulmonary cases—2+. 1 pleurisy twice +; recovery.
Klopstock and Seligmann	1914	49	0	0	0	0	0	A. M.	2 c.c. in each of 2 pigs.	Gross and microscopic.	
Lehmann.....	1914	104	6	6	2	1	50	A. M.	1-2 c.c.	Gross lesions.	1 tuberculosis of cheek and hand +. 1 scrofula and healed bone tuberculosis +. 2 occult tuberculosis +. 1 pulmonary tuberculosis +.
Rautenberg.....	1914	5	0	0	0	0	0	A. M.	5 c.c.	Injected apes and guinea-pigs.	Advanced pulmonary cases.
Seidenberger and Seitz	1914	26	9	35	7	6	85	P. M.	5 c.c.	Gross lesions.	
Storath.....	1914	17	0	0	0	0	0	A. M.	5-10 c.c.	Gross and microscopic. All rabbits.	Before and after tuberculin.
Austrian.....	1915	25	0	0	0	0	0	A. M.	4-7½ c.c.	Pulmonary cases.
Hamman.....	1915	20	0	0	0	0	0	A. M.	2½-5 c.c.	Pulmonary cases.
Brown et al.....	1915	84	3	4	0	0	0	A. M.	8-10 c.c.	Gross lesions.	Pulmonary cases.
Moewes.....	1915	80	9	11	10	5	50	1, P. M. 79, A. M.	2½-3½ c.c. Some 20 c.c.	Not given.	10 miliary cases. 70 pulmonary cases.
Rumpf and Zeissler	1915	25	2	8	0	0	0	Not stated.	Histological lesions.	Pulmonary cases.
Total.....	1508	195	12.9	48	32	66.6	

the results of several investigators who were not sufficiently critical in their interpretation of tuberculous lesions in guinea-pigs. If the series of Liebermeister, Sturm, and Kennerknecht are omitted, there remain 1345 cases with 119 positive inoculations, approximately 8.8 per cent. Faber, selecting 1060 cases tested by guinea-pig inoculation with blood obtained during life, found only 4.2 per cent positive, while in 37 cases tested post mortem 38 per cent were positive.

If one considers only cases of miliary tuberculosis the percentage of positive guinea-pig inoculations with blood becomes much higher. Of 48 cases of miliary tuberculosis listed in Table I 32 gave positive results, or 66.6 per cent. These figures are probably reliable, because in nearly all instances gross lesions were reported in the inoculated animals. If the cases of miliary tuberculosis are subtracted from the total number, there remain 1297 cases with 87 positive inoculations,

a percentage of 6.7 for all types of tuberculosis other than miliary tuberculosis.

One may conclude, therefore, that the occurrence of tubercle bacilli in the circulating blood, at least in sufficient number to infect a guinea-pig, is relatively infrequent (6.7 per cent) in all forms of tuberculosis other than miliary tuberculosis, whereas in miliary tuberculosis, tubercle bacilli occur in the blood in a large percentage (66.6 per cent) of cases.

The attempted demonstration of tubercle bacilli in the blood by means of stained smears needs little comment. Austrian and Hamman in 1915 published a detailed article with a fairly complete bibliography on the subject, and Berry in her article has good summaries of the earlier literature. Liebmman in 1891 reported the finding of tubercle bacilli in blood smears from tuberculin-treated patients. It was shown, however, that his findings were due to gross errors in technique.

Interest in the subject was reawakened in 1909, by the publications of Rosenberger in this country and of Schnitter in Germany. Rosenberger reported the demonstration of tubercle bacilli in the blood in 100 per cent of a series of 49 cases, and later of 300 cases, by staining the organisms in the centrifugalized sediment from citrated blood. Schnitter used a modification of Stäubli's acetic-acid method for the demonstration of parasites in the blood. After hemolyzing the red blood cells in acetic-acid he digested the sediment, obtained by centrifugalization, with antiformin. He claimed to have found tubercle bacilli in smears from the sediment so obtained in 32 per cent of tuberculous cases.

Following these publications a large amount of work was done on the subject with very conflicting results. Kurashige even found tubercle bacilli in blood from apparently normal persons. Parallel experiments with guinea-pig inoculations and staining methods did not, in most instances, give corresponding results. A source of error in these results was pointed out first by Brem, who demonstrated the frequent presence of acid-fast bacilli in distilled water. This observation was later confirmed by other writers (Burvill-Holmes, Beitzke, A. Lehmann). Bacmeister and Reuben found that the chemical reaction of acetic acid and antiformin may cause appearances simulating acid-fast bacilli, and Bernard, Debré, and Baron found acid-fast granules in pure antiformin. These observations, together with the conflicting results obtained from parallel series of guinea-pig inoculations, indicate the unreliability of the method.

The frequent difficulty in the differential diagnosis of miliary tuberculosis from other non-tuberculous infections clinically, and the slowness and uncertainty of diagnosis by guinea-pig inoculation, suggested the use of cultural methods for the demonstration of tubercle bacilli in the blood.

A fairly extensive review of the literature reveals only one case in which tubercle bacilli have been cultivated from the blood of tuberculous patients. This was a case reported by Faber, who obtained a growth of tubercle bacilli on a plain agar slant inoculated with blood from the heart of a child dead of generalized tuberculosis. Faber obtained negative cultures with 1 to 5 c. c. of blood in 21 other cases of miliary tuberculosis in children, and negative cultures have been obtained from the blood by Brown, Heise, and Petroff in 22 pulmonary cases, and by Anderson in 47 pulmonary cases and one joint case. Positive cultures from the blood of experimentally infected guinea-pigs and rabbits have been reported by Loewenstein, and later by Anderson.

The following method, suggested by Dr. Paul W. Clough, was used at first in my cultures, but was later modified in order to decrease the time necessary for growth to become apparent. Ten to 15 c. c. of blood were aspirated with a syringe from a cubital vein and added to an equal volume of 1½ per cent solution of sodium citrate to prevent clotting. Part of this blood was used to control guinea-pig inoculations in most of the cases. The remaining blood was added to shallow flasks of 5 per cent glycerine broth made neutral or slightly acid (phenolphthalein). After a preliminary incubation the

contents of the flasks were centrifugalized and the sediment planted on blood-agar slants. Human blood agar was used because it was simply and easily obtained. The slants were then sealed with paraffine to prevent drying, and incubated.

Positive results were obtained by this method in three cases.

CASE 1.—G. H. (Med. No. 23207), colored boy, 5 years of age. A clinical diagnosis of acute miliary tuberculosis was made, though at first the clinical picture resembled that of typhoid fever. Autopsy diagnosis: Acute miliary tuberculosis with the primary focus in the mediastinal glands, rupturing into the azygos vein. The blood culture was obtained 10 days before death. Three c. c. of citrated blood were added to a flask of glycerine broth and incubated for six weeks. Smears made from the sediment in the flask at this time showed acid-fast bacilli. The contents of the flask were then centrifugalized, part of the sediment planted on blood-agar slants, and part injected intraperitoneally into each of two guinea-pigs. After three weeks a dry, wrinkled, slightly brownish growth was noted on the blood-agar slants, and after six weeks one of the guinea-pigs died with generalized tuberculosis. Tubercle bacilli were demonstrated in smears from the subcultures, and from the organs of the guinea-pig, and were grown in culture from the spleen and liver of the guinea-pig. The other guinea-pig, inoculated with the sediment, died four days after the injection without tuberculous lesions.*

CASE 2.—G. W. (Med No. 35610), white man, 37 years of age. In this case also the clinical picture at first resembled that of typhoid fever, but the subsequent course made a definite diagnosis of miliary tuberculosis possible. Autopsy diagnosis: Fibrinous pleurisy, encapsulated apical pulmonary tuberculosis, bronchial lymphadenitis, caseous tuberculosis of the left adrenal, caseous mesenteric and retroperitoneal tuberculosis, rupture of a caseous gland into the cisterna chyli, generalized miliary tuberculosis, tuberculous meningitis and choroiditis, ulcer of the ileum. Fifteen c. c. of blood were obtained in citrate solution 14 days before death. A guinea-pig inoculated intraperitoneally with 3 c. c. of the blood died a few days later without tuberculous lesions. Twelve c. c. of the blood were added to several flasks of glycerine broth, and incubated for about five weeks. The contents of the flasks were centrifugalized, and the sediment planted on blood-agar slants which were then sealed. About four weeks later numerous pin-head-sized, buff-colored, dry colonies were noticed. Smears from the culture showed slender, acid-fast bacilli, some curved and beaded, typical of the tubercle bacillus in their morphology and arrangement. Three guinea-pigs were injected with varying amounts of the culture, and all developed generalized tuberculosis. At autopsy all of the animals showed caseous tissue at the points of inoculation, extensive glandular enlargement with caseation in many of the glands, and caseous conglomerate tubercles in the spleens, which in two of the guinea-pigs were six to eight times the normal size. Two of the guinea-pigs showed also similar caseous tubercles in the liver. Typical tubercle bacilli were demonstrated in the glands, spleens, and livers of all the inoculated guinea-pigs. Subcultures from the original culture were made, and a characteristic growth appeared in about 10 days. Smears from this growth showed typical tubercle bacilli in pure culture.

CASE 3.—J. E. (H. L. H. Disp. No. 12893), white boy, 6 years of age, from the service of Dr. Howland. Clinical diagnosis: Acute generalized miliary tuberculosis, tuberculous meningitis, and tuber-

* This blood culture, and several of the cultures from other fluids included in Table II, were taken by Dr. Paul W. Clough, and the data in regard to them obtained, with his permission, from the hospital records.

culosis of the choroid. No autopsy was made. X-ray examination showed miliary tuberculosis of the lungs. Tubercle bacilli were demonstrated by smears and by guinea-pig inoculation in the spinal fluid. The blood culture was made three days before death. Fifteen c. c. of blood were obtained in citrate solution. Two guinea-pigs were inoculated in the left groin with $3\frac{3}{4}$ c. c. of blood each. One guinea-pig lived four months and when killed at the end of that time, showed no tuberculous lesions. The other guinea-pig remained healthy for four months and was then lost. The other half of the blood ($7\frac{1}{2}$ c. c.) was added to shallow, glycerine, broth flasks. After 16 days the contents of the flasks were centrifugalized, the sediment planted on blood-agar slants and the slants sealed. This culture was set aside after a short period of observation, and was not looked at again until six months later, when a growth was noticed on one slant in the water of condensation. Characteristic, large, buff-colored, dry colonies were present in the fluid, and also at the base of the slant where the water of condensation had washed over the slant. Smears from the growth showed an acid-fast bacillus having the morphological features of the tubercle bacillus. An emulsion made from the growth was injected into two guinea-pigs. One of these died 18 days later with a large caseous mass at the site of inoculation, enlarged but not caseous iliac, mesenteric, and bronchial glands, marked enlargement of the spleen which was studded with miliary tubercles, and consolidation of the left lung. Typical tubercle bacilli were demonstrated in smears from the spleen. The other guinea-pig died six weeks after inoculation with caseation at the point of injection, general glandular enlargement with caseation, and extensive miliary tuberculosis of the spleen and liver. Smears from the liver and spleen showed many tubercle bacilli. Subcultures from the original culture were made, and a typical growth appeared in about nine days.

In carrying out these cultures no attempt was made to make an early diagnosis of the cases by means of the cultures, and they were not watched carefully for the first appearance of growth. In order to make the cultures of practical value in diagnosis it seemed desirable to try methods which would yield growth in a shorter period of time. In the third case cited above, the appearance of growth in only one of the slants inoculated from the broth after 16 days incubation suggested that very little multiplication had occurred in the broth. It was thought, then, that this preliminary incubation in broth might be dispensed with, and the following method was used. The blood was hemolyzed with distilled water, and the sediment after centrifugalization planted directly on blood agar slants which were sealed with paraffine.

Since there were no cases of miliary tuberculosis in the clinic at the time, the experiment was made with normal blood artificially seeded with a very small number of tubercle bacilli (G. W., third transfer). Ten cubic centimeters of blood were collected in the usual way, and the red blood corpuscles hemolyzed by the addition of distilled water. The blood was then centrifugalized at high speed for $1\frac{1}{2}$ hours, and the sediment planted on blood-agar slants which were sealed with paraffine. In six days growth became visible as small, semi-transparent colonies, which in eight days were somewhat larger and more opaque, and at the end of 10 days were characteristic. Growth in the culture direct from the body would probably have been somewhat slower in appearing than in this culture from the third transfer. Smears from the culture showed tubercle bacilli in pure culture.

Three positive cultures were obtained by the second method in two cases. In one of these cases two positive blood cultures were obtained, one ante mortem, and one from the heart's blood post mortem.

CASE 1.—E. M. (H. L. H. Disp. No. 14950), colored girl, 8 years of age, from the service of Dr. Howland. Clinical diagnosis: Generalized miliary tuberculosis, tuberculous meningitis. Autopsy diagnosis: Generalized tuberculous lymphadenitis, generalized miliary tuberculosis, tuberculous meningitis and peritonitis. Focus of dissemination not found. A blood culture was obtained one day before death. Twenty c. c. of citrated blood were hemolyzed by the addition of distilled water. The blood was then centrifugalized and four-fifths of the sediment (representing 16 c. c. of blood) was planted on blood agar slants. One-fifth of the sediment (from 4 c. c. of blood) was injected subcutaneously into the groin of a guinea-pig. This animal died three months later from an intercurrent bronchopneumonia without tuberculous lesions. In this case hemolysis of the blood was incomplete, and the slants were covered with a rather thick layer of sediment. For this reason growth did not become evident for 25 days. Smears from this growth showed typical tubercle bacilli. A guinea-pig inoculated with a suspension of this growth died 10 weeks later, and showed a general glandular enlargement with caseation in many of the glands, and a marked enlargement of the spleen, which was full of tubercles. The nature of these lesions was confirmed by microscopical sections. Tubercle bacilli were grown from the spinal fluid in this case in 10 days.

CASE 2.—Ten c. c. of blood were obtained from the heart of the preceding case at autopsy, and cultured in the same way. Growth became evident 13 days after the culture was made as small, colorless, non-characteristic colonies, and smears from the culture showed numerous tubercle bacilli. The spinal fluid obtained post mortem was also cultured. After 13 days growth was noted as fair-sized, buff-colored, dry, rounded colonies.

CASE 3.—L. M. (H. L. H. Disp. No. 15068), white girl, 4 years of age, from the service of Dr. Howland. Clinical diagnosis: Pulmonary tuberculosis, tuberculous meningitis, miliary tuberculosis (?). No autopsy was obtained. The blood was cultured one day before death. Ten c. c. of blood were obtained in citrate solution, and the red blood cells laked by the addition of distilled water. After centrifugalization three-quarters of the sediment was planted on blood-agar slants which were then sealed, and one-quarter of the sediment inoculated subcutaneously into the groin of a guinea-pig. After a week's incubation, minute, semi-transparent, colorless colonies became visible on some of the slants, and smears from these colonies showed clumps of typical tubercle bacilli. The guinea-pig inoculated with one-quarter of the sediment died $5\frac{1}{2}$ weeks later, and showed caseous areas in the regional and iliac glands. Tubercle bacilli were demonstrated in smears from these glands. A guinea-pig inoculated with a suspension of the growth is still alive after three weeks, but shows marked enlargement of the regional glands. An exploratory operation showed extensive caseation of the regional glands, and marked enlargement of the spleen, which was firm and apparently studded with small tubercles. The spinal fluid from this case was also cultured, and definite colonies appeared in a week.

By this method of cultivation positive results have been obtained from the blood in a relatively short time in two cases. A tentative diagnosis might have been made even before the appearance of visible growth by means of smears, if sufficient multiplication had occurred. When the colonies first appear they are not characteristic, and smears must be made before an absolute diagnosis can be made. It may be a long time before the growth becomes as profuse as that of old labora-

TABLE II.—CULTURES FROM TUBERCULOUS FLUIDS.
BLOOD CULTURES.

Name.	Hospital No.	Age.	Diagnosis.	Autopsy.	Smears.	Culture. Result and interval.	Guinea-pig inoculation. Result and interval.	Remarks.
G. H.	Med. No. 23207	5	Miliary tuberculosis.	Yes.	Not done.	+. 2½ mos.	Not done.	Guinea-pig inoculated with culture developed tuberculosis. 1 guinea-pig died prematurely.
G. W.	Med. No. 35610	37	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 2½ mos.	Done. Guinea-pig died prematurely.	Guinea-pig inoculated with culture developed tuberculosis.
J. E.	H. L. H. Disp. No. 12893	6	Miliary tuberculosis. Tuberculous meningitis.	No.	Not done.	+. 5 mos.	0. 2 guinea-pigs inoculated. Both remained well.	Guinea-pig inoculated with culture developed tuberculosis.
E. M.	H. L. H. Disp. No. 14950	8	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 25 days.	0. 1 guinea-pig inoculated. Died after 3 mos. without tuberculous lesions.	Guinea-pig inoculated with culture developed tuberculosis. Spinal fluid culture +.
E. M.	H. L. H. Disp. No. 14950	8	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 13 days.	Not done.	Blood culture made post mortem. Spinal fluid culture +.
L. M.	H. L. H. Disp. No. 15068	4	Miliary tuberculosis. Tuberculous meningitis.	No.	Not done.	+. 7 days.	+. 5½ weeks.	Guinea-pig inoculated with culture developed tuberculosis. Spinal fluid culture +.
H. L.	H. L. H. Disp. No. 14215	7 mos.	Miliary tuberculosis. Tuberculous meningitis. Pulmonary tuberculosis.	Yes.	Not done.	0.	0. Guinea-pig well after 5 mos.	Only 2 c.c. of blood obtained. Spinal fluid culture +.
S. Ht.	Med. No. 23684	26	Miliary tuberculosis. Tuberculous meningitis. Pulmonary tuberculosis.	Yes.	0.	0.	0.	Spinal fluid culture +.
W. S.	Med. No. 36896	18	Tuberculous peritonitis.	Yes.	Not done.	0.	Not done.	
E. L.	Med. No. 24140	5	Pulmonary tuberculosis. Tuberculous adenitis.	No.	Not done.	0.	Not done.	
C. M.	Med. No. 23487	24	Pulmonary tuberculosis.	No.	Not done.	0.	Not done.	
W. M.	Med. No. 23576	23	Pulmonary tuberculosis.	Yes.	Not done.	0.	Not done.	Spinal fluid culture 0.
M. S.	H. L. H. Disp. No. 13349	3	Tuberculous meningitis.	Yes.	Not done.	0.	0.	Few old tubercles in organs at autopsy.
C. T.	Med. No. 24277	8	Tuberculous meningitis.	Yes.	Not done.	0.	Not done.	Spinal fluid culture +.
M. H.	Med. No. 23799	20	Tuberculous meningitis.	Yes.	Not done.	0.	0.	Spinal fluid culture 0.
S. Hn.	Med. No. 23508	5	Tuberculous meningitis.	No.	Not done.	0.	0.	Spinal fluid culture +.
J. J.	H. L. H. Disp. No. 15178	1	Pulmonary tuberculosis. Tuberculous meningitis.	No.	Not done.	0.	0.	Spinal fluid culture +.

PLEURAL FLUIDS.

D. M.	Med. No. 23118	21	Pleurisy with effusion. Pulmonary tuberculosis (?).	No.	0.	+. 2 mos.	+. 2 mos.	
D. K.	Med. No. 23144	13	Pleurisy with effusion. Pulmonary tuberculosis (?).	No.	0.	0.	0.	
J. C.	Med. No. 23167	35	Pleurisy with effusion.	No.	0.	0.	0.	
A. S.	Med. No. 23365	51	Pleurisy with effusion.	No.	Not done.	0.	0.	

PERICARDIAL FLUIDS.

J. L.	Med. No. 23393	33	Syphilis of aorta with multiple aneurisms. Chronic adhesive pericarditis. Pleurisy with effusion, etc.	Yes.	0.	0.	Probably not tuberculous.
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TABLE II.—CULTURES FROM TUBERCULOUS FLUIDS.—CONTINUED.
SPINAL FLUIDS.

Name.	Hospital No.	Age.	Diagnosis.	Autopsy.	Smears.	Culture. Result and interval.	Guinea-pig inoculation. Result and interval.	Remarks.
S. Hn. Med. No. 23508		5	Tuberculous meningitis.	No.	Not done.	+ 5 wks.	Not recorded.	One 0 and 2 + cultures.
S. Ht. Med. No. 23684		26	Miliary tuberculosis. Tuberculous meningitis.	Yes.	+	+ 5 wks.	+	2 + cultures. Blood culture 0.
M. L. Med. No. 23922		2	Tuberculous meningitis.	No.	Not done.	+ 4 wks.	Not done.	
J. F. Med. No. 24005		2	Tuberculous meningitis.	No.	+ later.	+ 3-4 wks.	Not done.	First culture 0. 2 + cultures.
B. A. Med. No. 24036		8	Tuberculous meningitis.	Yes.	Twice 0.	+ 3 mos.	Not done.	2 + cultures.
O. H. Med. No. 24110		17	Tuberculous meningitis. Miliary tuberculosis. Tuberculosis of spine.	Yes.	0.	+ 2 mos.	Not done.	
G. R. Surg. No. 24203		8	Tuberculous meningitis.	Yes. (partial).	0.	+ 5 wks.	Not done.	
C. T. Med. No. 24277		8	Tuberculous meningitis.	Yes.	0.	+ 3 wks.	Not done.	
J. J. H. L. H. Disp. No. 15178		1	Tuberculous meningitis. Pulmonary tuberculosis.	No.	0.	+ 6 wks.	+ 3 mos.	
E. C. Med. No. 38345		41	Tuberculous meningitis. Pulmonary tuberculosis.	No.	0.	+ 6 wks.	Done. Guinea-pig died prematurely.	
H. L. H. L. H. Disp. No. 14215		7 mos.	Miliary tuberculosis. Tuberculous meningitis.	Yes.	+	+ 11 days.	Not done.	Guinea-pig inoculated with culture developed tuberculosis.
E. M. H. L. H. Disp. No. 14950		8	Tuberculous meningitis. Miliary tuberculosis.	Yes.	0.	+ 10 days.	Not done.	Guinea-pig inoculated with culture developed tuberculosis. Blood culture +.
L. M. H. L. H. Disp. No. 15068		4	Tuberculous meningitis. Miliary tuberculosis.	No.	+	+ 7 days.	+ 3 wks.	Guinea-pig showed tuberculosis only in regional and iliac glands. Blood culture +.
R. A. H. L. H. Disp. No. 2945		4	Tuberculous meningitis. Miliary tuberculosis (?).	No.	+	+ 7 days.	+ 4 wks.	Guinea-pig showed tuberculosis only in regional and iliac glands.
W. G. Med. No. 23453		5	Tuberculous meningitis.	No.	Not done.	0.	Not done.	
M. H. Med. No. 23799		20	Tuberculous meningitis.	Yes.	0.	0.	Not done.	Blood culture 0.

JOINT FLUIDS.

J. C. Surg. No. 23121	58	Tuberculous arthritis of knee. Pulmonary tuberculosis.	+	+ 3 wks.	Guinea-pig died in 10 days without lesions.	Tissue at operation tuberculous.
F. D. Surg. No. 23960	20	Villous arthritis of knee.	No.	Not done.	+ 3 mos.	Not done.	
S. W. Surg. No. 24214	47	Tuberculous arthritis of ankle.	No.	Not done.	0.	Not done.	

ABSCESS OF RIB.

L. C. Surg. No. 23966	50	Tuberculosis of rib. Abscess of chest wall, tuberculous.	Not done.	+ 4 wks.	Not done.	Tissue tuberculous.
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PERITONEAL FLUIDS.

W. W. Med. No. 23717	35	Cirrhosis of liver. Chronic gastritis.	0.	0.	Probably not tuberculous.
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ABSCESS OF NECK.

J. L. Surg. No. 24168	63	Abscess of neck, tuberculous. Healed tuberculosis of hip.	No.	Not done.	+ 6 wks.	Not done.	Abscess probably arising in sternoclavicular joint.
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tory strains, or this may occur only after repeated transfers. In the first case, the sediment obtained after laking the blood, when spread over blood-agar slants, was so thick that growth did not become recognizable for 25 days. In order to obtain positive cultures in the shortest possible time (therefore making the method more useful as a diagnostic procedure), it may be desirable to reduce the bulk of the sediment still further by digestion with antiformin (as originally suggested by Uhlenhuth and Kersten for cultures from sputum and other tuberculous material) and inoculation of the washed sediment directly on blood agar. This method would also be of value if the blood had accidentally become contaminated, or in the case of autopsy blood cultures where post-mortem invasion of the blood by other organisms may have occurred. Blood cultures done by this method are in progress at the present time. It is also possible that the use of other media, such as Dorset's egg medium, or glycerine beef agar, might give positive results in a shorter period of time, and in a larger percentage of cases. Human-blood-agar was used in my cultures because it was easily available.

Negative blood cultures by one or another of these methods were obtained in two out of the seven cases of acute miliary tuberculosis studied. In one of these cases only 2 c. c. of blood were available for culture, and 1 c. c. for guinea-pig inoculation. The guinea-pig has remained healthy for five months, and has no enlargement of the inguinal glands.

Negative blood cultures were obtained in nine cases of other types of tuberculosis, and guinea-pig inoculations done in four of these cases were negative as well. Of these cases one was a tuberculous peritonitis; a second, an acute tuberculous broncho-pneumonia; a third, a chronic pulmonary tuberculosis in the second stage; a fourth, a pulmonary tuberculosis with adenitis and tabes mesenterica; and the remaining five, cases of tuberculous meningitis.

Cultures from the sediment obtained by centrifugalizing other tuberculous fluids have also been made by planting the sediment directly upon blood agar slants and sealing them. The results of these cultures, and of control smears and guinea-pig inoculations when made, are recorded in Table II.

In the work summarized in Table II no attempt was made to watch the cultures for the earliest date at which growth appeared, except in the last four positive spinal fluid cultures in the table, and parallel smears and guinea-pig inoculations were not done in every case. Of the 16 spinal fluid cultures two were negative and 14 were positive. In seven of the cases positive by culture, tubercle bacilli could not be demonstrated in smears. Four pleural fluids were cultured with one positive result. Smears from this positive case were negative, but a guinea-pig inoculated with the fluid developed generalized tuberculosis. The three negative cases were negative also by guinea-pig inoculation, and two of the three by smears as well. Tubercle bacilli were grown in culture from two out of three fluids from tuberculous joints, and from the pus from an abscess of a rib and an abscess of the sternum. One peritoneal fluid and one pericardial fluid were negative by culture and by guinea-pig inoculation. Both of these cases were probably not tuberculous.

SUMMARY AND DISCUSSION.

In this work tubercle bacilli have been grown in culture for the first time from the circulating blood of five patients with miliary tuberculosis.

In the first method used the blood was added to glycerine-broth flasks, and after a preliminary incubation the sediment was planted on blood-agar slants, which were sealed and incubated. Three positive cultures were obtained by this method. In order to shorten the period of time necessary for growth to become visible, a second method was tried in which the blood was hemolyzed with distilled water and the centrifugalized sediment planted directly on blood agar slants. Three positive cultures were obtained from two patients by this method in 25, 13, and 7 days. In order to reduce still further the bulk of the sediment, and hence the period of time necessary for growth to become visible, a third method is suggested consisting in the digestion of the sediment by means of antiformin. Further work is being done with this method.

In order to be of value, cultural methods for the demonstration of tubercle bacilli in the blood must give positive results sooner and more constantly than the method of guinea-pig inoculation. The data at hand are insufficient to permit any definite conclusions, and further work is being done as cases are available, to determine these points. The experiment with the artificially seeded blood culture, and the three positive cultures obtained by the second method, indicate that growth may be obtained with appropriate methods in from one to three weeks. This is considerably under the time within which a positive result could usually be obtained by guinea-pig inoculation. The injection of blood subcutaneously into the groin of a guinea-pig produces an induration which will mask the development of a moderate glandular enlargement for several weeks, and prevent an early diagnosis of inoculation tuberculosis in this way. Furthermore, tuberculosis produced in guinea-pigs by the injection of blood containing tubercle bacilli may be very slow in developing, as claimed by Marmoreck in his work with experimentally infected guinea-pigs, and by others, using the blood of human cases. (Baetge, Rumpf and Zeissler.)

As regards the relative constancy with which results can be obtained by culture and by guinea-pig inoculation, nothing definite can yet be said. Under favorable cultural conditions, one might expect that one organism in the blood would produce a growth, while an appreciable number (varying inversely with the virulence) are needed to infect a guinea-pig. In the third case in my series half of the blood was injected into two guinea-pigs, neither of which became infected, while growth was obtained from the half cultured; and in the fourth case in which the blood culture was positive, the guinea-pig inoculated with one-fifth of the blood obtained died of intercurrent disease at the end of three months with no evidences of tuberculosis. Furthermore, guinea-pigs may die too soon for the development of macroscopic or microscopic lesions, either from the effects of the injection or from some intercurrent disease. This occurred in four of the control guinea-pig inoculations, one with blood, one with spinal fluid, one with joint fluid, and one with culture. The evidence at hand, then, would

indicate that suitable cultural methods will probably yield positive results more promptly and more regularly than animal inoculations.

The methods of demonstrating tubercle bacilli in the blood by means of smears have been shown to be unreliable, but when cultures are obtained from the blood we have conclusive evidence of the existence of a bacillemia.

On the other hand smears made from clear fluids with relatively little sediment frequently give reliable results by direct staining methods. In this series, however, tubercle bacilli were demonstrated more frequently by culture than by smears, as one would expect with favorable cultural conditions if the number of organisms is small. In the examination of one pleural fluid and seven spinal fluids for tubercle bacilli by smears and by culture, the smears were negative while the cultures were positive. In no instances were smears positive without the culture being positive also.

The practicability of blood cultures as a diagnostic method will depend upon the frequency with which the tubercle bacillus enters and persists in the blood stream. That bacillemia occurs frequently in miliary tuberculosis is shown by the high percentage (66.6 per cent) of positive results obtained by various authors in these cases by the method of guinea-pig inoculation with blood (Table I), and by the relatively large number of positive cultures obtained in the small series reported here (five out of seven cases). On the contrary this is probably a relatively uncommon phenomenon in pulmonary, and other forms of localized tuberculosis. Out of 1297 cases collected in Table I, only 6.7 per cent of guinea-pig inoculations with blood gave positive results, and in my series all of the blood cultures in these cases were negative.

In spite of the large amount of work which has been done on the subject of bacillemia in tuberculosis there is very little information which is based upon reliable methods of study. It has been shown definitely that tubercle bacilli may enter the blood stream, but relatively little is known as to the conditions in which bacillemia occurs, its frequency and regularity, the number of organisms present, or its diagnostic or prognostic significance.

The conditions in experimental tuberculosis in animals are somewhat better understood because the exact pathological lesions present can be determined, and to certain extent controlled. The bacillemia following the injection of tubercle bacilli has been studied by various investigators by the inoculation of guinea-pigs with blood from the infected animals. Some authors (for example Moewes) obtained positive inoculation tuberculosis by the injection of blood from experimentally infected animals in a large percentage of cases, while others in similar experiments obtained negative results (Sawyer). These divergent results are probably to be explained partly by differences in the virulence of the infecting organism, in its dosage and mode of administration, and in the time elapsing after inoculation before blood was withdrawn for the test. Marmoreck in 1907 published a detailed report upon this point. He found that after intravenous injection into guinea-pigs, the bacilli disappear from the blood after one to two days and recur four to six weeks later; after arterial

inoculation they disappear after one to two days and recur 5 to 14 days later. After subcutaneous inoculation bacilli appear for the first time in the blood after 30 to 60 days, following inoculation into the anterior chamber of the eye, somewhat sooner; and still earlier (14 to 20 days) after intraperitoneal injection. The relation of the virulence of the bacilli injected to their persistence in the circulation was studied by Hess, who found that the feebly virulent strains persist less long in the circulation after inoculation, and reappear later than do virulent strains.

Tuberculosis, as it commonly occurs in man, is not exactly analogous to that produced experimentally in animals, and a similar study of the bacillemia in human tuberculosis would be desirable. Blood cultures repeated at frequent intervals, supplemented, perhaps, by guinea-pig inoculations, would seem to offer a favorable method for determining not only the existence of a bacteriemia, but, approximately at least, the number of organisms present.

Blood cultures, then, are suggested as an aid in the differential diagnosis of acute miliary tuberculosis from other, non-tuberculous, infections and as a means of studying bacillemia in all forms of tuberculous disease. Direct cultures from spinal, pleural, peritoneal, and other fluids are recommended in those cases in which tubercle bacilli cannot be demonstrated by smears.

REFERENCES.

- de Amicis, M.: *Internat. Centralbl. f. d. gesammte Tuberkuloseforschung*, 1913, VII, 645. Beobachtungen über das Vorkommen der Tuberkelbazillen im kreisenden Blut. (Translation.) (Kongress für allgemeine Pathologie zu Pisa, März 27, 1913.)
- Anderson, J. F.: *Treas. Dep. Pub. Health and Mar.-Hosp. Serv., U. S. Hyg. Lab., Bull. No. 57, Wash., 1909.* The Presence of Tubercle Bacilli in the Circulating Blood in Clinical and Experimental Tuberculosis.
- Austrian, C. R., and Hamman, L.: *Johns Hopkins Hosp. Bull.*, 1915, XXVI, 293. Concerning the Occurrence of Tubercle Bacilli in the Circulating Blood.
- Bacmeister: *Münch. med. Wchnschr.*, 1913, LX, 343. Virulente Tuberkelbazillen im Blut nach der diagnostischen Tuberkelin-injection.
- Bacmeister and Reuben: *Deutsche med. Wchnschr.*, 1912, XXXVIII, 2350. Ueber "sekundäre" Tuberkulose.
- Baetge: *Deutsche med. Wchnschr.*, 1914, XL, 591. Ist der Nachweis von Tuberkelbazillen im Blute diagnostisch verwertbar?
- Baumgarten, P.: *Centralbl. f. d. med. Wissensch.*, 1881, XIX, 274. Zur Contagiosität der Tuberkulose.
- Beitzke, H.: *Berl. klin. Wchnschr.*, 1910, XLVII, 1451. Eine Fehlerquelle bei der Antiforminmethode.
- Bergeron, A.: *Thèse de Paris*, 1904. Etude critique sur la présence du bacille de Koch dans le sang.
- Idem*: *Presse méd.*, 1905, CXXXI, 129. Le bacille de Koch et le sang des tuberculeux.
- Bernard, Debré, and Baron: *Bull. Soc. d'étude scient. sur la tuberc.*, 1912, II, 154. Cited by Berry.
- Berry, J. L.: *J. Infect. Dis.*, 1914, XIV, 162. Tubercle Bacilli in the Blood.
- Bogasau, P.: *Internat. Centralbl. f. d. gesammte Tuberkuloseforschung*, 1912-1913, VII, 644. Tuberkelbazillen im Blute. (Referat.)
- Brem, W. V.: *J. Am. M. Assoc.*, 1909, LIII, 909. Investigation of Blood for Tubercle Bacilli. Contamination of Distilled Water with Acid-fast Organisms a Source of Error.

Brown, L., Heise, F. H., and Petroff, S. A.: Ztschr. f. Tuberk., 1915, XXIV, 97. Ueber das Vorkommen von Tuberkelbazillen im Blute von Patienten mit Lungen-tuberkulose.

Burvill-Holmes, E.: Am. J. M. Sc., 1910, n. s., CXXXIX, 99. A Study of the Alleged Presence of Tubercle Bacilli in the Circulating Blood.

Dailey, M. A.: Boston M. and S. J., 1909, CLXI, 318. On the Presence of Tubercle Bacilli in the Blood in Tuberculosis.

Dreesen, H.: Med. Klin., 1913, IX, 580. Ueber das Vorkommen von Tuberkelbazillen im strömenden Blut.

Elsässer, J.: Beitr. z. Klin. d. Tuberk., 1913, XXVI, 367. Tuberkelbazillen im Blutstrom bei Lungentuberkulose.

Faber, H. K.: J. Am. M. Assoc., 1914, LXIII, 1656. A Culture of Bacillus Tuberculosis from the Blood Post-Mortem of a Case of Miliary Tuberculosis.

Fischer, E.: Ztschr. f. Hyg. u. Infektionskrankh., 1914, LXXVIII, 253. Ueberlegungen und Untersuchungen zur Frage des Vorkommens von Tuberkelbazillen im strömenden Blut.

Fraenkel, C.: Internat. Centralbl. f. d. gesamte Tuberkuloseforschung, 1912-1913, VII, 316. (Referat.) Das Vorkommen von Tuberkelbazillen im Blut bei Lungentuberkulose.

Idem: Deutsche med. Wchnschr., 1912, XXXVIII, 2056. (Referat.)

Fraenkel, E.: Schmidt's Jahrb., 1913, CCCXVII, 201. Nachweis von Tuberkelbazillen im strömenden Blut. (Sammelreferat.)

Idem: Deutsche med. Wchnschr., 1913, XXXIX, 737. Tuberkelbazillen im Strömenden Blute.

Gary, A.: Thèse de Lyon, 1905. Bacilles de Koch dans le sang.

Haga, I.: Centralbl. f. Bakteriologie (etc.), I. Abt., 1913, LVII, Ref., Beiheft, 289. Diskussion. Reported by Möllers, Freinvereingung für Mikrobiologie, 1913.

Haas, W.: Beitr. z. klin. Chir., 1914, XC, 78. Ueber den Nachweis von Tuberkelbazillen im strömenden Blut bei chirurgischen Tuberkulosen.

Hess, A. F.: Arch. Int. Med., 1912, X, 577. The Relation of the Virulence of the Tubercle Bacillus to Its Persistence in the Circulation.

Huguenin, B.: Centralbl. f. Bakteriologie (etc.), I. Abt., 1908, XLVIII, Orig., 394. Nachweis von Tuberkelbazillen im Blute eines Fötus.

Jousset, A.: Semaine méd., 1903, XXIII, 153. Des septicémies tuberculeuses. (Review.) (Soc. méd. des Hôpitaux, Mai 8, 1903.)

Idem: Semaine méd., 1904, XXIV, 289. La bacillémie tuberculeuse.

Kachel: Beitr. z. Klin. d. Tuberk., 1913, XXVIII, 275. Ueber Tuberkelbazillen im strömenden Blut.

Kennerknecht, K.: Beitr. z. Klin. d. Tuberk., 1912, XXIII, 265. Ueber das Vorkommen von Tuberkelbazillen im strömenden Blut bei Kindern.

Klemperer, F.: Berl. klin. Wchnschr., 1914, LI, 436. Tuberkelbazillen im strömenden Blute.

Klopstock, F., and Seligmann, E.: Ztschr. f. Hyg. u. Infektionskrankh., 1914, CXXVI, 77. Zur Frage des Vorkommens von Tuberkelbazillen im strömenden Blut.

Kühnau: Ztschr. f. Hyg. u. Infektionskrankh., 1897, XXV, 493. Ueber die Resultate und die Leistungsfähigkeit der bakteriologischen Blutuntersuchung im Dienste der klinischen Diagnostik.

Kurashige, T.: Ztschr. f. Tuberk., 1911, XVII, 347. Ueber das Vorkommen des Tuberkelbazillus im strömenden Blute der Tuberkulösen.

Lange und Lindemann: Centralbl. f. Bakteriologie (etc.), I. Abt., Ref., 1913, LVII, Beiheft, 285. Ueber Tuberkelbazillen im strömenden Blut.

Lehmann, A.: Deutsche med. Wchnschr., 1913, XXXIX, 1556. Eine Fehlerquelle bei der Antiforminmethode.

Lehmann, P.: Beitr. z. Klin. d. Tuberk., 1914, XXX, 477. Ueber das Vorkommen virulenter Tuberkelbazillen im strömenden Blut bei Kindern.

Liebermeister, G.: Virchow's Arch. f. path. Anat. (etc.), 1909, CXCIV, 332. Studien über Komplikationen der Lungentuberkulose, und über die Verbreitung der Tuberkelbazillen in den Organen und im Blut der Phthisiker.

Idem: Med. Klin., 1912, VIII, 1018. Ueber sekundäre Tuberkulose.

Liebmann, V.: Berl. klin. Wchnschr., 1891, XXVIII, 97. Tuberkelbazillen im Blute von Kranken, die mit dem Kochschen Mittel behandelt wurden.

Löwenstein, E.: Ztschr. f. Tuberk., 1905, VII, 491. Ueber Septikämie bei Tuberkulose.

Lüdke: Wien. klin. Wchnschr., 1906, XIX, 949. Ueber den Nachweis von Tuberkelbazillen im Blut bei den Lungentuberkulosen.

Marmoreck, A.: Berl. klin. Wchnschr., 1907, XLIV, 18. Beitrag zur Kenntnis der tuberkulösen Septikämie.

Mayer, A.: Ztschr. f. Tuberk., 1913, XXI, 447. Ueber das Vorkommen von Tuberkelbazillen im strömenden Blute und in der menschlichen Milch.

Meisel, W.: Wien. med. Wchnschr., 1884, XXXIV, 1187. Vorkommen von Tuberkelbazillen im Blute bei der allgemeinen akuten Miliartuberkulose.

Moewes, C.: Deutsche med. Wchnschr., 1914, XL, 491. Tuberkelbazillen im Blut. II. Experimentelle Untersuchungen. (Tuberkelbazillen im Blute von Meerschweinchen.)

Idem: Deutsche med. Wchnschr., 1915, XLI, 1368. Tuberkelbazillen im Blute. III. Tuberkulinwirkung und Bazillämie.

Nobécourt and Darré: Bull. Soc. d'étude scient. sur la tuberc., 1912, II, 176. Cited by Berry.

Querner, E.: Münch. med. Wchnschr., 1913, LX, 401. Ueber Vorkommen von Tuberkelbazillen im strömenden Blut.

Rautenberg, E.: Deutsche med. Wchnschr., 1914, XL, 492. III. Zur Frage der Bazillämie bei Tuberkulose.

Rosenberger, R. C.: Am. J. M. Sc., 1909, n. s. CXXXVII, 267. The Presence of Tubercle Bacilli in the Circulating Blood in Tuberculosis.

Rist, Armand-Delille, and Lévy-Bruhl: Bull. Soc. d'étude scient. sur la tuberc., 1913, III, 9. Cited by Austrian and Hamman.

Rothacker, A., and Charon: Centralbl. f. Bakteriologie (etc.), I. Abt., 1913, LXIX, Orig., 478. Das Vorkommen von Tuberkelbazillen im strömenden Blut.

Rumpf, E.: Münch. med. Wchnschr., 1912, LIX, 1951. Ueber das Vorkommen von Tuberkelbazillen im Blutstrom.

Rumpf, E., and Zeissler, J.: Deutsche med. Wchnschr., 1915, XLI, 185. Ueber das Vorkommen von Tuberkelbazillen im Blut.

Sawyer: Arch. Int. Med., 1909, IV, 628. Tubercle Bacilli in the Blood.

Schnitter: Deutsche med. Wchnschr., 1909, XXXV, 1566. Nachweis und Bedeutung der Tuberkelbazillen im strömenden Phthisikerblut.

Seidenberger and Seitz: Virchow's Arch. f. path. Anat. (etc.), 1914, CCXV, 89. Ueber das Vorkommen von Tuberkelbazillen im Herzblute bei chronischer, lokalisierter und latenter Tuberkulose.

Stäubli, C.: Münch. med. Wchnschr., 1908, LV, 2601. Beitrag zum Nachweis von Parasiten im Blut.

Storath, E.: Ztschr. f. Tuberk., 1914, XXII, 1. Ueber Bedeutung und Auftreten virulenter Tuberkelbazillen im Blut nach der diagnostischen Tuberkulininjection.

Sturm: Beitr. z. klin. d. Tuberk., 1911, XXI, 239. Tuberkelbazillen im Blute von Tuberkulösen.

Uhlenhuth, P., and Kersten: Ztschr. f. exper. Path. u. Therap., 1909, VI, 759. Eine neue Methode zum culturellen und mikroskopischen Nachweis von Tuberkelbazillen im Sputum und anderem tuberkulösen Material.

de Verbizier, A.: Rev. de méd., 1913, XXXIII, 161. Nouvelles recherches sur la présence du bacille de Koch dans le sang circulant des tuberculeux.

Villemin: Etudes sur la tuberculose. Paris, 1868. Cited by Jousset.

FIBROID TUMORS OF THE VULVA.

A REPORT OF 12 CASES AND A DIGEST OF THE LITERATURE ON THIS SUBJECT.

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Fibroid tumors of the vulva, although rather uncommon, are by far the most frequent of the benign, solid neoplasms found in this region. An idea of their frequency may be gathered from the fact that but six cases have appeared among 23,000 gynecological admissions to The Johns Hopkins Hospital.

The tumor usually appears first as a small, firm, painless nodule immediately beneath the skin of the labium majus. Its growth may be extraordinarily rapid, and the tumor usually soon becomes pedunculated. Growth continues and actual interference with locomotion may be the first inconvenience experienced by the patient.

When seen by the surgeon these tumors have in most cases developed a well-marked pedicle, and, hanging between the thighs, present a most remarkable picture. The upper surface of the tumor and the skin of the pedicle may be covered by hair. The skin covering the tumor is generally thick and thrown into numerous shallow folds and wrinkles at once suggesting the skin of the scrotum. The skin is freely movable over the tumor and its surface is usually quite unbroken. On palpation a firm, smooth or slightly lobulated mass is made out which is quite insensitive to moderate pressure. One or more pulsating vessels may be felt in the pedicle. On pulling the tumor and thereby making tension on the pedicle, a tough fibrous cord may sometimes be made out traversing the pedicle and entering the inguinal canal.

As the tumor grows the circulation may be impaired and the growth become oedematous and semi-fluctuant to palpation. The wrinkles and folds in the skin then disappear, the surface of the tumor becomes smooth and shiny and ulcerations commonly appear at the most dependent portion. In many cases the tumor undergoes just these changes during menstruation. The tumor may swell to twice its size during the menstrual period (Penrose¹⁰²), become soft and quite sensitive and rapidly assume its former size, firm consistency and relative insensitiveness soon after the cessation of menstruation. Should pregnancy occur the tumor usually shows the same changes, but in addition may take on a very rapid growth.

The remarkable resemblance of some of these tumors, especially those of the labium majus, to the scrotum, has been commented upon frequently in the literature.

In at least one case (Coates²⁸), a diagnosis of hermaphroditism was made, the firm, rounded elastic tumor being mistaken for a testicle.

Fibromata developing in the extraperitoneal portion of the round ligament have led to the most frequent mistakes in diagnosis.

A tumor appearing in this region has often been mistaken for an inguinal hernia (Heidemann,⁶⁵ Von Recklinghausen,¹¹¹ Verneuil,¹³² etc.), and in some instances the patient has worn a truss until the increase in size demanded surgical intervention (Doormann³⁵). This is perhaps not surprising, for a tumor in this region may appear very much like an inguinal hernia and may even be reducible through the inguinal canal (Nebesky⁹⁴). In addition there may actually be a hernia in association with the tumor of the round ligament, as reported by Hecker,⁶⁴ Hofmorkel,⁶⁶ Landau,⁷⁶ etc.

Ordinarily fibroid tumors of the vulva cause no symptoms, other than the inconvenience dependent upon their size and weight and, if pedunculated, by their chafing and interference with locomotion. The tumor may become swollen and sensitive during menstruation and pregnancy and, if ulcerations follow the oedema usually associated with the increased vascularization under these circumstances, infection may render the tumor quite sensitive. The same sensitiveness may develop should the tumor undergo malignant change, a rather frequent outcome, in which event it usually ulcerates. Even the large sessile fibroids of the vulva rarely cause pain or pressure symptoms. Those developing in the rectovaginal septum may cause constipation, and in one case reported by Villiers and Damage¹³⁹ retention of urine was caused by the pressure of a calcified fibroid of the vestibule on the urethra. Itching has been mentioned occasionally as a prominent symptom (Ill⁶⁸).

As the tumor increases in size it may render coitus practically impossible (Coates²⁸), while interference with parturition has been reported by Albert.¹

Etiology and Pathology.—With very rare exceptions fibroid tumors of the vulva occur within the child-bearing period. Esser,⁴¹ Polaillon¹⁰⁵ and Weber¹⁴⁰ have each reported a case in which the tumor probably developed after the menopause, while Goldreich,⁵⁶ in 1909, presented a case of a pedunculated fibroma of the right labium in a nursing baby. That such exceptions are rare is probably due to the marked influence which menstruation and pregnancy exert on these tumors.

Fibroid tumors of the vulva grow more rapidly and attain greater size than superficial fibroid tumors in any other part of the body, while those originating in the subperitoneal areolar tissue and usually appearing first at the vulva are the real "giant" tumors of pathology, being the largest tumors known to the literature (Whitney and Harrington¹⁴¹).

That tumors of the vulva are subject to a marked periodic increase in blood supply in association with menstruation is plainly evident from the changes, such as swelling and tenderness, which have often been noted during the period.

Again, during pregnancy they are subject to a prolonged increase in blood supply and in consequence usually take on a very rapid growth.

These tumors may develop from the connective tissue of almost any of the vulval structures, such as the subcutaneous connective tissue of the labium majus or labium minus. They may likewise take their origin in the extraperitoneal portion of the round ligament or in some pelvic structure such as the subperitoneal areolar tissue, and growing in the direction of least resistance may appear at the vulva in the region of the labium majus, perineum or buttock.

Fibroid tumors of the vulva are more prone to degenerative processes than similar tumors in any other part of the body. This is due to two factors. These tumors are subjected to marked variations in their blood supply during menstruation and pregnancy, which cause a rapid growth. Growing rapidly, the majority soon become pedunculated, that is, they develop ideal mechanical conditions for degenerative processes. Edema, lymphangiectases, hyaline and cystic degeneration, calcification, ulceration and infection as well as gangrene and both myxomatons and sarcomatons metamorphoses, have all been reported in the literature.

Before discussing the histogenesis and mode of growth of these tumors I shall report briefly the cases which have appeared in this clinic, and the specimens which have been sent to the laboratory of gynecological pathology.

CASE I.—Gyn. No. 21735. I. F., aged 17, colored.

Clinical History.—The family and personal histories were unimportant. The patient had never been pregnant. Menstruation began at the age of 15 and continued normally.

Present Illness.—About one year before admission the patient noticed a very small firm swelling just to the right of the vaginal orifice. It had been growing rapidly ever since. It itched occasionally but otherwise there was "no feeling in it." At times the tumor would swell slightly. The only discomfort was caused by its size and weight, and its interference with locomotion.

Examination (Fig. 1).—Springing from the lower portion of the right labium majus is a large pear-shaped pedunculated tumor measuring 19 cm. in length. The tumor part is quite distinct from the pedicle and is 14 cm. in length by 9.8 cm. in its greatest diameter. The pedicle measures 4.8 cm. in length and 1.3 cm. in diameter at the tumor and 2.3 cm. at the base. The surface of the tumor is covered with normal-looking skin except at the lower extremity, where there is a small ulceration 1 cm. in diameter. The surface temperature is normal.

The tumor is soft and feels somewhat lobulated. There is no superficial sensation on pinching or tapping the surface. On squeezing the whole mass between the hands, the patient complains of discomfort. There are several crypt-like depressions in the skin over the upper part of the tumor, measuring 1 or 2 mm. in depth.

The pedicle contains no palpable vessels. There is no hair on the surface of the tumor, but there is a small amount scattered over the base of the pedicle. No cord-like structure can be felt in the pedicle, and traction on it shows that there is no connection with the round ligament or with any structure in the upper portion of the labium or the canal of Nuck.

Operation.—Simple amputation at the vulva by an oval incision 2 x 3 cm. about the base of the pedicle. No large vessels encountered. Convalescence uneventful. Healing per primam.

Pathological Description.—On section, a soft, pearly white, somewhat translucent surface is presented from which a quantity of clear limpid fluid exudes on slight pressure. Three small cystic cavities are seen, containing the same clear fluid. The largest of these measures 9 mm. in diameter, and is limited by a definitely calcified wall. Here and there rather large vessels are seen, the walls of which are thickened and for the most part partially calcified. In one place a completely calcified vessel is seen, and can be traced about an inch.

Scattered over the surface are numerous, very small cystic spaces containing clear fluid, and giving certain areas of the cut surface a spongy appearance. The cut surface of the pedicle shows a few blood-vessels, but no fibrous cord.

Microscopic Examination.—The skin covering the tumor is quite normal. Near the pedicle normal skin elements, such as hair follicles and sweat glands, are seen. These are not present in the skin over the rest of the tumor.

The body of the tumor is quite cellular and is made up of connective-tissue cells arranged in loose strands running in all directions. In places the cells are widely separated. The cytoplasm is spindle-shaped or branching. The nuclei are round, oval or spindle-shaped and are vesicular. There are extensive areas of hyaline degeneration throughout the tumor.

The larger cystic spaces are lined with a single layer of endothelium and their thickened fibrous walls are undergoing calcification.

The smaller spaces seen in the spongy areas described above, are dilated lymphatics and are very numerous. They are lined with a single layer of endothelium.

The blood-vessels are fairly numerous. There is a scant round-cell infiltration about a few of the smaller vessels. The walls of the larger vessels are thickened and some are becoming calcified.

In one area a very small group of smooth muscle fibers is found.

The pedicle is made up of rather dense bundles of connective tissue and a few bands of smooth muscle, both showing marked hyaline degeneration. A number of large blood-vessels are seen, some of which appear quite normal, others showing thickened walls, hyaline degeneration and calcification.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated, with lymphangiectases, extensive hyaline degeneration and beginning calcification.

CASE II. Gyn. No. 10670. V. T., aged 40, colored.

Clinical History.—The family and personal histories were of no importance. She had had one child 23 years before admission to the hospital. After a normal menstrual life the menopause had appeared three years before with typical symptoms.

Present Illness.—Eight years before admission a small red itching nodule appeared on the left labium majus. For six years it grew very slowly but quite steadily. During the two years before admission the tumor rapidly increased in size.

During the menstrual periods the tumor had usually become swollen and sensitive. Since the complete cessation of menstruation the tumor had continued to show periodical monthly changes. At the same time each month the tumor would become greatly swollen and very sensitive. At the end of four or five days the swelling and sensitiveness would disappear, the tumor resuming its usual shape and size. Otherwise there had been no discomfort except rather marked interference with locomotion.

Examination.—Suspended from the left labium majus is a pear-shaped pedunculated tumor covered with normal skin. In appearance the tumor is very similar to that seen in Case I (Fig. 1), except that it is somewhat larger and is attached to the left instead of the right labium majus. There are no ulcerated areas. From the base of the pedicle the tumor measures 22 cm. The pedicle is 7 cm. long and 2 cm. wide; the tumor is 15 cm. long and 8.5 cm. in its greatest diameter.

On palpation the tumor is found to be rather soft and is not lobulated; no cord-like structure can be made out in the pedicle. No sensation is caused by squeezing the tumor.

Operation.—Under local anæsthesia (Schleich), the tumor was removed by an elliptical incision about the base of the pedicle. Closure with silk. Healing per primam.

Pathological Description.—The surface of the tumor is covered with normal skin which is thrown into numerous shallow folds giving it the appearance of a scrotum. There are no ulcerations. A few large hair follicles are visible in the region of the pedicle.

On section a smooth white glistening translucent surface presents which is homogeneous throughout. On pressure a small quantity of clear fluid exudes from the cut surface. There are no areas of softening or cystic change.

Microscopic Examination.—The tumor is composed of pure fibrous tissue, the bundles of fibers showing a marked tendency to arrange themselves in parallel strands. The strands of fibers are loosely arranged and in places the tissue is seen to be definitely œdematous. There is extensive hyaline degeneration throughout. Everywhere the tissue is poor in cells. What nuclei there are, are oval or spindle-shaped, quite pale and vesicular. The blood-vessels are of moderate size and number. The smaller vessels are for the most part surrounded by limited but dense round-cell infiltrations. Next one of the larger vessels is a clump of fat cells. Beneath the normal skin which covers the tumor there is a slight round-cell infiltration. No smooth muscle fibers are seen in the body of the tumor.

The pedicle contains a number of large blood-vessels and a few strands of smooth muscle; the skin in this region contains a number of hair follicles.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated, with œdema and extensive hyaline degeneration.

CASE III. Gyn. No. 8518. E. H., aged 22, white.

Clinical History.—The family and personal histories were unimportant. The patient was single. She began to menstruate at 14. The periods were somewhat irregular at times, the interval varying from 3 to 5 weeks. The flow had always been scant, of 4 or 5 days' duration and attended with considerable pain.

Present Illness.—Six years before admission to the hospital the patient noticed a lump in the lower portion of the left labium majus, about the size of the "last joint of the thumb." For four years the growth was steady but slow. During the two years before admission to the hospital the tumor rapidly increased in size. There had been no discomfort except the inconvenience to locomotion and occasional chafing. No changes in the tumor had been noted during menstruation, and it had remained of about the same consistency from the first.

Examination (Fig. 2).—The left labium majus forms the base of a large pedunculated tumor. The pedicle occupies the entire labium. From a point opposite the clitoris the tumor measures 16 cm. in length. From a point opposite the fourchette (lower portion of the base of the pedicle) it measures 11 cm. in length. The tumor itself is 7 cm. in diameter at its widest point. On palpation the mass is made out to be definitely lobulated and rather soft. It is covered with normal skin, which in the region of the pedicle and about the base of the tumor is covered with normal labial hairs. The pedicle contains some large pulsating vessels.

Operation.—The tumor was removed by an elliptical incision about the base of the pedicle. Convalescence uneventful. Healing per primam.

Pathological Description.—The specimen consists of a rather soft nodular tumor covered with normal skin which is thrown into numerous folds giving it the appearance of a scrotum, an appearance which is accentuated by a number of rather large blood-vessels which can be seen just beneath the skin surface. The skin is but loosely attached to the underlying mass.

On section the bulk of the tumor is seen to be made up of a rather firm mass measuring 7 cm. in diameter. The cut surface is smooth, homogeneous, pearly white, glistening and translucent, and on pressure a small amount of clear fluid exudes. Surrounding this main nodule are 15 or 20 smaller but similar ones. These vary from a few millimeters to 2.5 cm. in diameter and all show the same characteristics on section.

Microscopic Examination.—The tumor is composed of fibrous tissue arranged in rather loose strands running in all directions, but here and there showing a definite tendency to become parallel. The entire tumor is quite cellular, the nuclei being large and vesicular and oval or spindle-shaped. Everywhere there is extensive hyaline degeneration. A very few large fat cells are scattered sparsely throughout the tumor tissue, there being usually not more than two or three in a single field and large areas of tissue completely devoid of any adipose elements. The blood-vessels are quite numerous and of moderate size. About some of them there is a moderate round-cell infiltration. No œdema. No smooth muscle.

Diagnosis.—Fibroma, labium majus, pedunculated, with hyaline degeneration and slight adipose infiltration.

CASE IV. Gyn. No. 3896. M. T., aged 32, white.

Clinical History.—The family and personal histories were unimportant. The patient had been married 11 years before admission to the hospital and had had one child. Menstruation became established at the age of 16 and had always been regular and normal except for rather severe pain on the first day.

Present Illness.—The patient first noticed a small hard lump in the left labium majus 18 months before admission. It was not sensitive. For a year it grew slowly, but for the six months preceding admission had taken on a very rapid growth. For three months it had been ulcerated and quite painful.

Examination (Fig. 3).—The vaginal orifice is occluded by a large semi-fluctuant tumor in the base of the left labium majus. The tumor is reddened, sensitive, and on its vaginal surface presents an ulcerated area from which blood is oozing. The tumor occupies the region of Bartholin's gland, is well circumscribed and does not infiltrate the tissues above or below. There is no enlargement of the inguinal glands.

Operation.—The tumor was excised with a wide area of skin about it and a considerable amount of the underlying areolar. The patient left the hospital in 12 days, the wound being healed except for a minute granulating area at the lower angle.

Pathological Description.—The specimen consists of a tumor nearly spherical in shape and measuring 5.5 x 4.5 cm.

One half of its free surface is covered with normal skin, the other half with vaginal mucous membrane. Springing from the vaginal surface near the muco-cutaneous border is a mass 3 x 2.5 cm. and projecting 1 cm. above the level of the mucosa. One half of this mass is smooth, the other half ulcerated and deeply excavated.

On section a striking picture is seen. Surrounding the entire tumor, with exception of the base of the mass projecting from the vaginal surface, is a narrow capsule of firm tissue composed of parallel fibers.

The central portion of the tumor, which measures 3.7 cm. in diameter, is sharply differentiated from the surrounding tissue. It is of a much lighter hue and is composed of a loosely arranged fibrillated meshwork, crossed by a few fine bands of somewhat denser and darker tissue.

Beneath the vaginal surface the capsule on section presents a crescentic surface extending from the ulcerated area at the muco-cutaneous border to the opposite pole of the tumor. Here the capsule has been split and separated into two layers by the invasion of tissue of a darker color than the other portions of the tumor. This layer of tissue is continuous with the ulcerated area

on the surface of the tumor, being composed of roughly parallel, loosely arranged fibers which, converging toward the ulcerated mass, radiate out to form it. This layer contains a few islands of very pale tissue, the largest of which measures 5 x 3 mm., similar to that composing the central portion of the growth.

Microscopic Examination.—With the exception of the nodule projecting from the surface, the tumor is surrounded by a distinct capsule, the free surface of which is covered by stratified squamous epithelium. The capsule is composed of parallel layers of connective tissue, which show marked hyaline degeneration. Just beneath the epithelium there is a moderate round-cell infiltration. Toward the skin surface bundles of non-striped muscle fibers, hair follicles, and other skin elements are present.

At the base of the nodule, at the muco-cutaneous border, the connective-tissue layer entirely ceases, but the epithelium continues a short distance over the sides of the nodule, the tumor then presenting a granulating surface.

The central portion of the tumor is composed of a meshwork of large spindle-shaped fibers, having spindle-shaped, or occasionally oval, vesicular nuclei. The greater portion of the tissue is rarefied, the cells very large and separated by a delicate blue-tinted substance. Running across the tissue in various directions are bands of denser formation containing blood-vessels of considerable size. The nuclei of these cells are, for the most part, spindle-shaped and vesicular, and about the size of the nuclei of smooth muscle fibers. There is, however, a considerable variation. Many of them are large, being three or four times the size of the others, oval and vesicular, and here and there are scattered cells containing exceedingly large, deeply staining nuclei, frequently vacuolated. Frequent irregular mitotic figures are found. Throughout the tissue there is a moderate round-cell infiltration, and in the looser portions are seen a number of mast cells. There is a fair vascular supply, the vessels being very thin-walled. The crescentic band of tissue running from the ulcerated portion to the opposite pole of the tumor is essentially the same as that just described, but here the fibers are densely packed. Scattered through it here and there are myxomatous areas of varying size.

At the base of the ulcerated nodule the cells become very abundant, and continuing directly into it form radiating strands to the surface. The nodule is very cellular and has a rich supply of blood-vessels, the surface being formed of capillary loops covered over with a dense layer of leucocytes.

Pathological Diagnosis.—Fibromyxosarcoma, labium majus.

CASE V. Gyn. No. 15229. M. A., aged 45, white.

Clinical History.—The family and personal histories were unimportant. She had been married 21 years and had borne nine children, the youngest of whom was 14. Menstruation began at 12 and had continued regular and normal up to the age of 42, since when the periods had become irregular.

Present Illness.—For several years the patient had noticed some small tumors near the vaginal orifice, which had gradually increased in size. They had never given any symptoms.

Examination.—Hanging from the left labium majus by a short pedicle measuring 5 mm. in diameter is a tumor measuring 7.5 cm. in length and from 5 to 6.5 cm. in diameter. The tumor is insensitive, is covered with normal skin and is dark purplish in color.

On the inner surface of the right labium majus there are two small but thick-walled cysts, one of which is open and infected.

There is a marked anterior relaxation with a large cystocele. The cervix is greatly hypertrophied. The uterus is of normal size and is in good position. The adnexa are normal.

Operation.—The tumor of the left labium was removed by an incision about the base of the pedicle. The two cysts in the right labium were then dissected out. Closure with catgut. Amputation of the cervix and anterior colporrhaphy were then completed.

Pathological Diagnosis.—Fibroma, labium majus. Pedunculated. Sebaceous cysts (two), labium majus. The specimen has been lost. No pathological description, therefore, can be given.

CASE VI. Gyn. No. 13733. A. C., aged 35, white.

Clinical History.—This patient, who had had three children, was admitted to the hospital for the treatment of a severe chronic endocervicitis. The cervix was cauterized and a small firm nodule measuring 1 cm. in diameter, which she had never noticed, was removed from the left labium majus. The tumor was embedded in the tissue of the labium.

Pathological Diagnosis.—Fibroma, labium majus.

CASE VII. Path. No. 22063. The abstract of the clinical history was kindly given us by Dr. Hunner, with whose permission this case is reported.

Clinical History.—The patient, a white woman, aged 47, a multipara, came to his office complaining of a small growth. She had had it for some time, but recently it had been getting sore and discharging pus, and for the past month had been bleeding at times.

Examination.—Showed a tumor of the left labium minus.

Operation.—After injecting the base of the pedicle with 1 per cent cocaine, the tumor was cut off with the Paquelin cautery and two pumping vessels controlled by dull heat.

Pathological Description.—The specimen consists of a small tumor removed from the left labium minus. Attached to a pedicle 13 mm. long and 8 mm. in diameter is a small, firm polypoid mass measuring 2.5 x 2 x 1.2 cm. The tumor is divided into two distinct lobules by a furrow 1 cm. deep. The entire surface is covered with thick, wrinkled skin and issuing from the depths of some of these wrinkles are a number of long hairs. There is a small ulcerated surface at the most dependent portion of the tumor.

On section, the cut surface near the pedicle is seen to be composed of very densely packed parallel strands of fibers which radiate out to form the tumor mass, which is composed of more or less loosely arranged fiber bundles running in various directions. In the central portion of the tumor these strands of tissue are separated by very numerous blood-vessels of considerable size, giving the surface a spongy appearance. The skin is seen to be distinctly thickened.

Microscopic Examination.—The very irregular surface is covered with a thick layer of normal squamous epithelium continuous over the entire tumor except at the ulcerated portion at the tip. Here there is a granulating surface thickly covered and infiltrated with leucocytes. The body of the tumor is made up of rather loosely arranged bundles of fibrous tissue widely separated in certain areas by numerous blood-vessels of considerable size. Throughout the entire tumor the fibrous strands show marked hyaline degeneration. The nuclei are abundant, and are for the most part spindle-shaped, but many large oval, vesicular forms are seen. Large areas throughout the tumor are heavily infiltrated with leucocytes and round cells.

Pathological Diagnosis.—Fibroma, labium minus, infected.

I wish to report briefly on the following specimens. In these cases no clinical history was obtainable, the specimens merely having been sent to the laboratory for diagnosis.

CASE VIII. Path. No. 4056. The specimen consists of a large multinodular tumor removed from the labium majus. The mass is composed of a large number of small, firm, round tumors varying in size from a pea to 4 cm. in diameter and surrounded by a small amount of adipose and connective tissue.

Microscopic Examination.—The different nodules are all of essentially the same structure. Each is surrounded by a definite capsule of parallel bands of dense fibrous tissue. The stroma is composed of loosely arranged connective-tissue cells, large and

spindle-shaped or fusiform, and containing large oval or spindle-shaped vesicular nuclei. In a few places there is a slight tendency to strand formation, but for the most part no such tendency is suggested. Here and there areas rich in cells alternate with masses of hyaline tissue containing practically no nuclei. The nuclei are for the most part pale and vesicular, but here and there a number of very deeply staining nuclei are seen with finely granular chromatin. A number of large pale cells with very large, rather deeply staining vesicular nuclei are seen. The tumor is for the most part definitely oedematous.

Pathological Diagnosis.—Fibroma, multinodular, labium majus, oedematous, with hyaline degeneration.

CASE IX. Path. No. 2682. The specimen consists of a round polypoid growth removed from the labium majus and measuring 1.5 cm. in diameter. The surface is covered with thick, wrinkled skin. There is a short pedicle about 4 or 5 mm. in length. The tumor has a firm consistency.

Microscopic Examination.—The surface of the tumor is irregular, consisting of small finger-like papillae covered with normal squamous epithelium. The cells of the deepest layer contain a golden brown, granular pigment.

The stroma is composed of fibrous tissue somewhat poor in cellular elements and containing a moderate amount of elastic fibers. There is no smooth muscle.

The cells, which are fairly evenly distributed throughout the tissue are long, spindle-shaped or branching, and contain large oval or elongated vesicular nuclei. Blood-vessels are fairly numerous and are of moderate size.

The superficial portions of the stroma show a slight round-cell infiltration.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated.

CASE X. Path. No. 3033. The specimen consists of a small nodule measuring 7 mm. in diameter, removed from the inner surface of the labium majus to which it was attached by a very short pedicle.

Microscopic Examination.—The surface is covered with normal squamous epithelium, which presents somewhat marked papillary elevations. The tumor itself is composed of a fibrous stroma, fairly rich in cells. These are oval, fusiform or branching and contain large oval or spindle-shaped vesicular nuclei. There are a few round cells scattered sparingly between the tumor cells. A few large round cells with faintly straining cytoplasm and densely stained nuclei are seen. The blood-vessels are small and moderate in number. There are no muscle cells.

Diagnosis. Fibroma, labium majus. Pedunculated.

CASE XI. Path. No. 2027. The specimen consists of three small calcareous nodules removed from the labium majus and measuring 5, 8 and 10 mm. in diameter. One was decalcified and sectioned.

Pathological Diagnosis.—Calcareous nodules from labium majus, probably calcified fibromata.

CASE XII. Path. No. 5513. This specimen was received from the Frauenklinik, Strassburg. It consists of a small cuboidal piece of tissue removed from a tumor of the right labium majus. The gross specimen was ovoid, somewhat larger than an egg and perfectly encapsulated. It had the consistency of a fatty tumor. On section, the cut surface bulged and was somewhat mottled, the whole having much the appearance of a testicle.

Microscopic Examination.—The tissue is quite homogeneous, consisting of fibrillated tissue quite rich in cellular elements. The cells are more or less spindle-shaped and have vesicular nuclei of various sizes. The nuclei differ greatly in the intensity with which they take the stain. Mitotic figures, for the most part irregular, occur in small numbers. The blood-vessels are fairly numerous.

Pathological Diagnosis.—Spindle-cell sarcoma, labium majus.

HISTOGENESIS AND MODE OF GROWTH.

Despite the fact that almost every possibility finds an illustrative case in the literature, there are certain very definite points of predilection from which the majority of fibroid tumors of the vulva develop. I have arranged these below in what appears to be their order of frequency.

GROUP I. *Fibroid Tumors Originating in the Subcutaneous Connective Tissue; 70 cases:*

- (a) of the labium majus; 53 cases.
- (b) of the labium minus; 11 cases.
- (c) of the vestibule and vagina; 5 cases.
- (d) of the perineum; 1 case.

GROUP II. *Fibroid Tumors Originating in the Extraperitoneal Portion of the Round Ligament; 39 cases:*

- (a) and growing outward into the labium majus; 25 cases.
- (b) and remaining in the inguinal canal; 11 cases.
- (c) and growing back into the abdomen; 2 cases.
- (d) and growing up between the layers of the abdominal wall; 1 case.

GROUP III. *Fibroid Tumors Originating in the Subperitoneal Connective Tissue and Appearing at the Vulva; 14 cases.*

GROUP IV. *Fibroid Tumors Originating in the Connective Tissue of Bartholin's Gland; 4 cases.*

GROUP V. *Fibroid Tumors Originating in Hematomata; 2 cases.*

GROUP VI. *Fibroid Tumors Originating in the Connective Tissue of the Rectovaginal Septum; 2 cases.*

GROUP I. FIBROID TUMORS ORIGINATING IN THE SUBCUTANEOUS CONNECTIVE TISSUE.

Fibroid tumors originating in the subcutaneous tissue of the vulva (Klob⁷³) include more than half of the cases in the literature. As will be seen, the vast majority appear in the labia and soon become pedunculated. Likewise, a considerable majority of the tumors of long standing show some form of degenerative change. In this connection a point of considerable importance is brought out by the analysis. Of the 64 cases of fibroid tumors of the labia majora and labia minora reported, 14 cases, or 22 per cent, showed a malignant (sarcomatous) metamorphosis. In one case (Weber¹⁴⁰) the sarcomatous change was definitely traced back to trauma.

In addition to the labia as a point of origin, rare instances have occurred in which the tumor has originated in the connective tissue of the vestibule (Churchill,²⁶ Parsons¹⁰⁰ and Thomas¹³²); of the vagina (Elisher and Hasenbalg), and of the perineum (Newman⁹⁵).

The following cases have been reported:

A. ORIGIN IN THE SUBCUTANEOUS TISSUE OF THE LABIUM MAJUS.

Albert.¹ A primipara, aged 25, nine months pregnant, showing a huge fibroma hanging from the left labium majus down to the knees.

Arcangelis.⁴ Para-II, aged 48, had noted a growth the size of a pea in the left labium majus three years before. When seen, a tumor the size of a seven months' foetal head was found hanging from the left labium by a pedicle 5 cm. long. Microscopic diagnosis, fibromyxosarcoma.

Bullard.²⁰ Para-II, aged 38, had found a small lump in the left side of the vulva two years previously. At present, a bag-like mass,

2 inches in diameter, is attached to the lower end of the left labium majus by a pedicle $\frac{1}{2}$ inch in diameter. Microscopic diagnosis, fibroma. The center of the tumor is composed of loosely meshed connective tissue, while that at the periphery is dense.

Burr.²² Para-IV, aged 42, had noticed a growth in the upper third of the left labium majus 18 years before. At the end of six years it had grown to the size of a walnut and was removed. Six years later the patient noticed a similar growth lower down in the labium majus, and later two more nodules appeared at the site of the first operation. The three tumors were removed and proved to be fibromata. Three years later there had been no recurrence.

Calmann.²³ A primipara, aged 22, in the fourth month of pregnancy, had had a small hard lump in the right labium majus, the size of a pea, since childhood. It had grown very slowly up to the time she had become pregnant, when it took on a rapid growth. On examination a tumor the size of an apple was found suspended from the middle of the right labium by a pedicle 10 cm. long and as thick as the little finger. Microscopic diagnosis, oedematous fibroma.

Canuyt et Princetau.²⁴ A woman, aged 29, had noticed a small tumor of the left labium majus one year before. A pedunculated tumor the size of a banana was removed, which proved to be a very vascular fibroma.

Eichholz.³⁹ A nullipara, aged 30, with a tumor of the left labium majus, 11 cm. long by 6 cm. broad. It had developed slowly from a small tumor first noticed at the age of three years. On removal, it was found to be a cavernous fibroma.

Esser.⁴¹ Case (a). A nullipara, aged 35, had noticed a hard lump the size of a bean in the right labium majus four years previously. Examination showed a tumor the size of a child's head attached to the labium by a pedicle 9 cm. long. There was an ulceration on the inner surface. The patient stated that during menstruation the tumor became swollen and painful. Microscopically, the tumor proved to be an oedematous fibroma.

Esser.⁴¹ Case (b). A woman, aged 51, with a tumor of two years' duration, found to arise from the left labium majus by a pedicle 3 cm. long. The tumor was about the size of a small pear. Microscopic diagnosis, fibroma.

Fürst.⁴⁷ Case (a). Para-II, aged 41, had noted a small wart-like prominence in the right labium majus 12 years previously. The tumor had grown steadily and would become swollen during menstruation. Examination showed a growth 13.5 cm. in circumference attached to the labium by a pedicle 8 cm. long by 1.5 cm. in thickness. Microscopic diagnosis, oedematous fibroma.

Fürst.⁴⁷ Case (b). Para-XI, aged 38, with a slow-growing tumor of the left labium majus the size of a duck's egg. Microscopic examination proved it to be a partly gangrenous spindle-cell sarcoma.

Gangolphe.⁴⁹ Para-V, aged 36, was found to have a fibromyoma embedded in the left labium majus. The patient stated that it would become swollen and sensitive during menstruation.

Garrigue.⁵⁰ removed a pear-shaped, pedunculated tumor from the left labium majus, which measured 8 by 7 by 4 cm. The pedicle was as thick as a finger. The tumor had begun to slough and emit a foul odor. Microscopic diagnosis, oedematous fibroma.

Giles.⁵⁵ Primipara, aged 22, six months pregnant, came complaining of a tumor which had appeared a few months before. Examination showed a tumor the size and shape of a fresh fig attached to the lower portion of the left labium majus by a long thin pedicle. On removal, "it presented all the characteristics of a molluscum fibrosum." Giles considered that this growth had originated during pregnancy.

Graefe.⁵⁷ Para-III, aged 36, was found to have a tumor of the left labium majus, the size of a man's fist, attached by a short pedicle as thick as the little finger. The tumor had been present five years but had taken on a rapid painful growth during the

past year. Microscopic diagnosis, fibroma, undergoing myxomatous change.

Grime.⁵⁹ Para-I, aged 41, showed an enormous pedunculated tumor of the right labium majus. It had been present for seven years and had begun to slough. The mass consisted of a number of tumors, the largest of which measured 25 inches in circumference, the next largest, 18 inches, and the third, 11 inches. A large number of smaller tumors varied in size from 3 by 2 inches to $1\frac{1}{2}$ by 1 inch. The tumors were composed of hard fibrous tissue. The pedicle contained a large pulsating vessel. Weight $16\frac{1}{2}$ pounds.

Handfield-Jones.⁶¹ operated on a woman, aged 28, who had a pedunculated tumor of the left labium majus, the size of a large foetal head, at term. It had been present five years and had recently become ulcerated. Its growth had been gradual. Microscopic examination showed it to be a "pure myxoma."

Holzmann.⁶⁷ removed a pedunculated fibroma weighing 6850 gm. from the right labium majus of a woman, aged 37. The tumor hung to the knees. Diagnosis, fibroma.

Ill.⁶⁸ describes a case in which he removed a number of small papillomatous growths from the vulva of a patient, aged 58. The tumors were scattered over the labia majora and vestibule, were of one year's duration and had caused no symptoms other than itching. Microscopically, the tumors proved to be papillomatous fibromata.

Kayser.⁷⁰ demonstrated a fibromyoma of the labium majus. The patient, aged 56, had passed the menopause two years previously. Although of only four years' duration, the tumor measured 34 cm. in circumference.

McClintock.⁸² A multipara, aged 40, with a tumor of the right labium majus, stated that it had been present for 15 years. The growth hung from the labium by a pedicle as thick as three fingers. It was about the size of an orange, ulcerated, and was found to be composed of fibrous tissue.

McDonald.⁸³ removed a myxoma of the right labium majus, which recurred during a subsequent pregnancy.

Marcano.⁸⁵ operated on a woman, aged 25, who had had a tumor of the left labium majus for four years. At operation, the tumor was found to be very vascular and to extend into the recto-vaginal septum. It was about the size of an orange. Microscopic diagnosis, fibromyoma.

Michon.⁸⁹ removed a hard, lobulated tumor from the right labium majus of a patient, aged 32. Microscopic diagnosis, fibroma.

Mond.⁹⁰ saw a patient with a tumor of the right labium majus the size of a child's head. Although of seven years' duration it had given no discomfort, the patient applying for treatment because she was about to marry. At operation the tumor was found to be extremely vascular. Microscopic diagnosis, fibromyoma.

Monod.⁹¹ Para-III, aged 30, had noted a nut-sized tumor in the left labium majus during her last pregnancy, six years previously. A sessile tumor was removed, which weighed 570 gm. and proved, on microscopic examination, to be a fibromyoma.

Morestin.⁹² Case (b). A woman, 71 years old, came to operation with a fibroma of the left labium majus of 10 years' duration. The tumor was as large as two fists and hung by a pedicle down to the knees.

Odelbrecht.⁹⁶ removed a hard tumor from the right labium majus of a woman 40 years of age. The tumor was larger than a man's fist and had developed in 10 months. At operation it was found to be embedded in the labium and reached up to the clitoris and down to the anus. It extended upward along the vagina half-way to the cervix. Microscopic diagnosis, fibroma.

Oreillard.⁹⁷ A patient, aged 27, complained of a tumor of the left labium majus of seven years' duration. The tumor had at first been sessile but had become pedunculated. Examination showed

a tumor 22 cm. in circumference, ulcerated on its inner surface and hanging by a pedicle 10 cm. long. Microscopic examination showed it to be a very vascular fibromyxoma.

Orloff⁹⁸ removed a spindle-cell sarcoma of two years' duration from the labium majus of a patient, aged 30. It weighed 100 gm.

Penrose.¹⁰² Six months after her delivery at term, eight years before, a patient, aged 41, para-II, noticed a small hard lump in the right labium majus, which had been growing steadily since. Examination showed a pear-shaped tumor the size of a fist hanging from the labium by a pedicle 10 inches long. The pedicle contained a pulsating artery the size of the radial and the patient stated that during menstruation the tumor would swell to twice its size. Microscopic examination showed a very vascular, œdematous fibroma, undergoing myxomatous changes.

Perewaloff¹⁰⁸ describes a 31-pound fibroma of the labium majus of seven years' duration. It hung to the knees.

Ponzian.¹⁰⁸ A patient, aged 35, para-VIII, had noticed a small tumor in the right labium majus 12 years before. Examination showed an ulcerated tumor the size of a pear hanging by a pedicle 5 cm. long. Microscopic diagnosis, fibroma.

Ritchie¹¹³ removed a small pedunculated tumor from the labium majus, which proved, on microscopic examination, to be a fibroma.

Rosenthal.¹¹⁴ A patient, aged 53, had noticed a small wart-like nodule on the right labium majus for a number of years. Six months previously it had taken on a rapid growth. Examination showed an ulcerated tumor the size of an apple hanging by a pedicle 4 cm. long and as thick as the little finger. Microscopic diagnosis, fibromyoma, showing recent myxomatous change.

Scanzoni¹¹⁸ removed a pedunculated fibroma the size of a man's fist, which hung from the right labium majus to the middle of the thigh. Aside from the swelling and sensitiveness during menstruation, the tumor had caused no symptoms.

Schiele.¹¹⁹ A patient, 26 years of age, had had a hard painless swelling in the left labium majus for 11 years. On examination a tumor the size of a child's head was found suspended from the lower portion of the left labium by a pedicle 2.7 cm. long. On section, two cystic cavities the size of an olive were found. Microscopic diagnosis, œdematous fibroma.

Schumann.¹²¹ Para-VI, aged 45, had noticed a small hard lump in the left labium majus for eight years. Its growth had been slow but steady. Examination revealed an ulcerated tumor the size and shape of a pear hanging from the labium by a pedicle 10 cm. long and 2 cm. in thickness. Microscopic diagnosis, myxomatous fibroma.

Schwajblmair¹²² describes a case in a woman 29 years of age, who developed in the course of four years a tumor of the left labium majus weighing 1740 gm. Microscopic diagnosis, myxofibroma.

Selcke¹²³ operated on a nullipara, aged 20, who had had a tumor of the left labium majus for three years. During the past year it had become pedunculated. The tumor measured 15 cm. in length and the pedicle, 4 cm. Microscopically it was composed entirely of fibrous tissue and showed a number of greatly dilated lymph spaces.

Simpson-Barbour.¹²⁵ Case (b). A virgin, aged 16, had noticed a swelling the size of a plum three years previously, in the right labium majus. The tumor was at first sessile but soon became pedunculated. It was ulcerated and had been bleeding, and had grown to the size of a large fist. Microscopic diagnosis, fibromyxoma.

Souligoux¹²⁹ removed a fibrolipoma, the size of an orange and of 14 years' duration, from the right labium majus.

Strina¹²⁸ operated on a patient, aged 24, showing a pear-shaped tumor measuring 7 by 4 cm. and hanging from the right labium majus by a pedicle 10 cm. long. A microscopic section proved it to be a fibromyoma in the initial stages of degeneration.

Szili¹³⁰ removed a tumor the size of a goose egg from the right labium majus of a patient, aged 37, para-IV, which had been present for four years. Microscopic diagnosis, spindle-cell fibrosarcoma, containing a number of giant cells.

Tarnier¹³¹ describes a case in which a large fibroma of the labium majus increased rapidly in size during pregnancy and after labor returned to its former dimensions.

von Tischendorf.¹³³ A virgin, aged 22, had noticed a tumor of the left labium majus seven years previously, which had grown steadily to the size of a fist and had become pedunculated. Microscopic examination showed it to be an œdematous fibroma. In places the skin epithelium showed rapidly proliferating basilar processes penetrating far downward.

Tuttle¹³⁴ operated on a woman, aged 52, para-III, who had noticed a painless lump in the right labium majus four years previously. It had grown steadily and had doubled in size in the last year. The only symptoms were from its weight and interference with locomotion. It proved to be a cystic fibroma 7½ inches long and 17½ inches in circumference.

Valude¹³⁵ removed a large tumor from the right labium majus of a patient, aged 45, para-III, who had first noticed the swelling eight years previously. Its growth had been more rapid during the last 18 months. Microscopic diagnosis, fibromyoma.

Van der Smissen¹³⁸ removed a pedunculated fibroma from the right labium majus of a virgin, aged 20. The tumor was the size of a dove's egg. Two years later he delivered the patient of a child at term and noticed five small fibromata which had developed in the left labium majus.

Villiers, de Hotman and Damage¹³⁹ describe a case of calcified fibroma the size of a hen's egg, removed from the upper portion of the right labium majus of a patient, aged 61. The tumor had caused retention of urine by compression of the urethra.

Zangemeister¹⁴³ removed a tumor the size of a potato from the left labium majus of a patient, aged 36, para-I. The patient had noticed it for 10 months. Microscopic diagnosis, fibromyoma.

Zielewicz¹⁴⁴ describes a sessile fibroma of the labium majus, occurring in a pregnant woman, which measured 59 cm. in circumference and weighed 2965 gm.

Zubrycki.¹⁴⁶ A patient, aged 38, para-VI, had noticed a small tumor of the left labium majus for four years. During the last pregnancy it had increased to the size of an apple, and had become pedunculated. Microscopic diagnosis, fibroma.

B. ORIGIN IN THE LABIUM MINUS.

Baer.⁹ A patient, aged 39, para-IV, had noticed, four years before, two small growths, each about the size of a mulberry, on either side of the clitoris. A few months later a number of similar growths appeared on both labia minora, and later still, the vaginal orifice, the perineum and anal orifice became similarly involved. All the growths were pedunculated. Microscopic examination proved them to be fibromata. They were composed entirely of connective tissue and showed nothing in common with skin papillomata or with elephantiasis except in macroscopic appearance.

Bell¹⁰ removed a pedunculated growth the size of an orange from the left labium minus of a patient, aged 56, para-VI. The tumor had been present six years. Microscopic diagnosis, spindle-cell sarcoma.

Bondi¹⁶ describes a small tumor, the size of a cherry stone, removed from the labium minus of a patient, aged 26. Histologic examination revealed the typical structure of a neurofibroma.

Bovée¹⁷ removed a pedunculated tumor from the right labium minus of a nulliparous negress, aged 26, which proved to be a fibroma.

Burgio.²¹ A patient, aged 29, had noticed a small tumor on the right labium minus for nine years. Examination showed a pinkish tumor the size of a dove's egg. Microscopic diagnosis, fibromyoma.

Collyer²⁹ reports a case of "fibroma diffusum" of the labia minora in a patient, aged 25, with active syphilis. Probably a case of elephantiasis.

Goldreich⁶⁶ demonstrated a case of a pedunculated fibroma of the right labium minus, the size of a hazelnut, in a baby 10 months old.

Grigorowitsch⁶⁸ describes a rare case of a woman, aged 29, showing an ulcerated tumor the size of a child's head attached to the right labium minus and a number of smaller tumors about the vaginal orifice. The principal tumor weighed 740 gm. and microscopic examination showed it to be a fibrosarcoma.

Kirchoff⁷² reports a most remarkable case of a girl, aged 18, who for some years had felt, when lifting any weight, that some large object was about to come out of the vagina. One day, when lifting a heavy weight, she experienced a sudden sharp pain at the vaginal outlet accompanied by a profuse hæmorrhage. Examination showed a freshly ruptured hymen and, hanging by a thick pedicle from the right labium minus, a large tumor reaching the middle of the thigh. The tumor mass was made up of a large number of fibroid nodules.

Legneu et Morel⁷⁹ report a case in which a very oedematous fibroma was removed from the right labium minus of a patient, aged 25, in the sixth month of pregnancy. It had been present one year but had recently grown very rapidly.

Prokess¹⁰⁹ removed a fibroma half the size of a man's fist from the labium minus of a patient, aged 38.

C. ORIGIN IN THE SUBMUCOUS CONNECTIVE TISSUE OF THE VESTIBULE AND VAGINA.

Churchill²⁶ removed a fibrolipoma situated just below the orifice of the urethra. The tumor measured 1 inch long and ½ inch thick.

Hasenbalg ("Zwei seltene Tumoren der weiblichen Geschlechtsorgane," *Zeitschr. f. Geb. u. Gyn.*, 1892, Bd. 23, p. 52). A tumor, which proved to be an oedematous fibroma, was found to fill the posterior vaginal vault to which it was attached by a pedicle. The patient was a virgin, aged 49.

Elischer ("Ein Fall eines Scheidenfibroms," *Cent. f. Gyn.*, 1893, Bd. 17, p. 846). A fibromyoma the size of a date was removed from the left side of the vagina of a nullipara, aged 40.

Parsons¹⁰⁰ reports a case of a woman, aged 30, showing a walnut-sized tumor of the vestibule projecting forward and pushing the urethra downward. The mass proved to be a fibromyoma undergoing hyaline degeneration and containing a small calcareous nodule.

Thomass¹³² removed a sessile tumor measuring 4.5 by 3 by 2.5 cm. from between the urethra and labium minus of a nullipara, aged 17. It had been noticed only three months. Microscopic diagnosis, fibroma.

D. ORIGIN IN THE SUBCUTANEOUS TISSUE OF THE PERINEUM.

Newman.⁹⁵ A patient, aged 30, para-V, with a pedunculated tumor of the perineum the size of a foetal head, stated that it had grown very rapidly during her last pregnancy. On removal it proved to be a fibroma.

GROUP II. FIBROID TUMORS ORIGINATING IN THE EXTRAPERITONEAL PORTION OF THE ROUND LIGAMENT.

The development of fibroid tumors in the extraperitoneal portion of the round ligament is not especially rare. Tumors developing in this region are among the most interesting of the benign vulval growths and have received considerable comment in the literature since attention was first drawn to them by Sänger¹¹⁷ in 1880. The tumor appears first in the inguinal

region and as it increases in size usually pushes forward into the labium majus and becomes pedunculated. It may remain in the inguinal region indefinitely, and be partially or completely reducible. On the other hand it may in rare instances grow backward through the internal abdominal ring (Nebesky⁹⁴ and Prang¹⁰⁷), or upward "between the layers of the abdominal wall" (Leopold⁸⁰).

As might be expected, a tumor originating in this portion of the round ligament is often found in association with an inguinal hernia. Fibroids of this origin show the same marked tendency towards sarcomatous change as noted in those originating in the subcutaneous connective tissue. Of the 39 cases in Group II, five cases, or 13 per cent, showed a malignant metamorphosis.

The following cases fall naturally into two main groups according to their mode of growth:

A. GROWING OUTWARD INTO THE LABIUM MAJUS.

Aschoff.⁵ A patient, aged 42, had noticed a small tumor in the upper end of the labium for a year and a half. At operation, an adenofibroma the size of an almond was removed from the inguinal canal.

Aumoine.⁷ Case (a). A patient, aged 26, para-I, had noticed a nut-sized tumor in the right inguinal region six months after her delivery, two and a half years previously. It had grown slowly into the upper end of the labium majus and had become pedunculated. It would become quite painful during menstruation. At operation, the tumor was found to arise in the round ligament and microscopic examination showed it to be a fibroma.

Aumoine.⁷ Case (b). A patient, aged 45, had noticed a slow-growing, pedunculated tumor of the right labium majus for four and a half years. Operation was refused but the author considered it to have originated in the extraperitoneal portion of the round ligament.

Blisner¹⁴ removed a fibromyoma the size of an apple from the left labium majus of a patient who had noticed the growth only a few months before. It had taken origin in the extraperitoneal portion of the round ligament.

Bochenski¹⁵ removed a large fibroma from the right labium majus and found it attached to the round ligament. It recurred after several years.

Clark²⁷ describes the case of a woman, aged 59, para-IX, who showed a tumor of the uterus and a firm, circumscribed, sausage-shaped mass in the left inguinal region projecting downward into the labium along the course of the round ligament. The mass was movable, but could not be pushed back into the abdomen. At operation a hysterectomy was completed and the inguinal tumor removed through a separate incision. The tumor of the uterus proved to be a round-cell sarcoma and the inguinal mass a fibromyoma of the round ligament measuring 8 by 6 by 4 cm.

Coates.²⁸ A patient, aged 21, para-I, had noticed an enlargement of the upper end of the left labium majus since her earliest recollection. Before marriage it had given no discomfort whatever but was now causing pain at coition. On examination a mass was found occupying the labium and inguinal canal and extending down to the anus. It bore a remarkable resemblance to a large scrotum and on palpation two ovoid tumors the size and consistency of testicles were made out. In fact, her physician had previously made a diagnosis of hermaphroditism and only marriage disclosed her true sexual identity. At operation a multinodular tumor measuring 17 by 8 by 6 cm., and attached to the round ligament, was removed. Microscopic diagnosis, fibromyoma.

Cullen.³⁰ A patient, aged 37, had noticed a tumor in the upper end of the right labium majus for a number of years, which had caused pain in the inguinal region at each menstruation. At operation a tumor of the extraperitoneal portion of the right round ligament was removed, which proved, on microscopic examination, to be an adenofibroma. Two years later the patient returned with a tumor in the left iliac region and laparotomy revealed an adenofibroma of the intraperitoneal portion of the left round ligament.

Duplay.³⁷ A patient, aged 52, para-I, had not menstruated for seven months. Eight months before she had noticed a small, rapidly growing tumor in the right inguinal region. Examination showed a tumor in the right labium majus the size of an ostrich's egg. On removal, it proved to be fibromyoma originating in the right round ligament and showing extensive myxomatous change.

Gemmel⁵² removed a fibroma the size of an orange from the labium majus of a patient, aged 44, para-X. At operation, the tumor showed considerable diffuse extension toward the inguinal canal and buttock. Microscopic examination showed the central portion of the tumor to be undergoing "a degeneration closely simulating sarcomatous change."

Géroulanos⁵³ reports a case in which a huge pear-shaped fibromyoma, weighing 8500 gm., hung to the knees by a thin pedicle attached to the labium majus. The tumor had probably taken origin in the extraperitoneal portion of the round ligament.

Guinard.⁶⁰ A multipara, aged 35, had noticed a multinodular tumor in the left inguinal region for 15 years. It had gradually grown downward into the labium majus. At operation a multinodular fibromyoma the size of an apple was removed from the extraperitoneal portion of the round ligament.

Hecker⁶⁴ reports the case of a patient, aged 40, who since early childhood had noticed a small tumor in the upper end of the right labium majus. It would become sensitive during menstruation. At operation, a myoma of the right round ligament, in association with a congenital hernia of the right ovary, was found.

Landau.⁷³ A patient, aged 59, para-II, had noticed a small nodule in the upper end of the left labium majus 20 years before. Examination revealed an enormous tumor of the labium hanging down to the knees, and measuring 65 cm. in circumference, in association with a large inguinal hernia which occupied the upper portion of the mass. Microscopic diagnosis, fibrolipoma.

Merkel⁸⁸ describes the case of a nullipara, aged 20, with a tumor the size of two fists, hanging to the middle of the thigh by a pedicle which issued from the left inguinal canal. It had been present 10 years. Microscopic diagnosis, myoma.

Morestin⁹³ removed a tumor of 15 years' duration from the left labium majus of a patient, aged 50. At operation, the pedicle, which was about the thickness of a finger, was found to arise in the inguinal canal. Microscopic diagnosis, fibromyoma.

Nebesky⁹⁴ (a). A patient, aged 40, para-VII, had noticed a tumor in the left labium majus 13 months before. At operation, a tumor the size of an apple, with a pedicle entering the left inguinal canal, was removed. Microscopic diagnosis, fibromyoma.

Paletta⁹⁹ removed a tumor the size of a fist from the upper portion of the left labium majus. The pedicle entered the inguinal canal and was attached to the round ligament. It contained a cystic cavity filled with clear limpid fluid. Microscopic diagnosis, fibroma.

Polaillon¹⁰⁵ describes the case of a multipara, aged 45, showing a pedunculated tumor of the left labium majus the size of a child's head and hanging to the middle of the thighs. The pedicle entered the inguinal canal. Microscopic diagnosis, fibromyoma.

Reboul.¹¹⁰ A patient, aged 45, para-III, had noticed a small tumor the size of a pigeon's egg, in the upper part of the right labium majus, for 16 years. At menstruation, the tumor would become

swollen and sensitive. At operation, a vascular fibromyoma of the extraperitoneal portion of the round ligament was found in association with a hydrocele of the canal of Nuck.

Von Recklinghausen¹¹¹ removed an adenofibroma of the extraperitoneal portion of the right round ligament of a patient, aged 49, para-V, who had complained of a tumor of the labium majus for a year and a half. It would become swollen and sensitive during menstruation and had previously been diagnosed as a hernia. It measured 3 by 3 by 2 cm.

Reverdin and Buscarlet.¹¹² A patient, aged 49, para-VII, had first noticed a tumor in the left labium majus the size of a nut. When seen, it had reached the size of a hen's egg and from its position and character on palpation appeared as a Bartholin gland cyst. At operation a fibromyoma, originating in the round ligament, was found.

Roustan¹¹⁶ removed a fibromyoma the size of an apple, from the left labium majus of a patient, aged 42, para-VII. The tumor was of 13 months' duration. It was found to have arisen in the extraperitoneal portion of the round ligament.

Weber.¹⁴⁰ Case (a). A patient, aged 58, had noticed a small hard tumor in the left inguinal region three years before. It had grown to the size of a goose's egg and had invaded the labium majus. A fibroma of the left round ligament was removed.

Weber.¹⁴⁰ Case (b). A young nullipara had noticed a tumor in the left inguinal region three years before, which had grown rapidly and become pedunculated. At operation it was found to have originated in the extraperitoneal portion of the round ligament. Microscopic examination showed the smaller part of the tumor, near the inguinal ring, to be a myoma, while the larger, more superficially situated portion, was a myosarcoma. The sarcomatous change was traced back to trauma.

B. REMAINING IN THE INGUINAL CANAL.

Doormann.²⁵ During her last pregnancy, five years before, a patient, aged 32, para-II, had noticed a small swelling in the right inguinal region. For three years she had worn a truss to hold it back. At operation, a fibroma of the round ligament, the size of an apple, was removed. It contained a number of cystic cavities filled with clear fluid.

Fischer.⁴² A nullipara, aged 24, had noticed a slowly growing tumor in the right inguinal region for a year and a half. It had become quite painful, especially during menstruation. At operation a fibroma of the round ligament was removed.

Hansemann⁶² demonstrated a case showing a myoma of the right round ligament in an inguinal hernia.

Heydemann.⁶⁶ A patient, aged 44, para-II, had noticed a tumor in the right inguinal region for a year. It would become very sensitive during menstruation. A diagnosis of irreducible inguinal hernia was made, but operation revealed a fibromyoma of the round ligament.

Hofmorkl⁶⁸ reports the case of a woman, aged 33, para-I, with a large, left-sided inguinal hernia near which a large hard tumor had appeared, causing gangrene of the overlying abdominal wall and the projecting parts. There was also a small pedunculated tumor of the left labium majus quite separate from the other mass. At operation, the larger tumor proved to be a fibroma of the left round ligament in association with an inguinal hernia. The small tumor was a fibroma of doubtful origin.

Von Mars.⁸⁰ A patient, aged 28, para-III, had noticed a painful point in the right inguinal region three years before. A year later a small tumor appeared which then grew rapidly. At operation, a fibromyoma the size of an ostrich's egg was removed from the inguinal region. The center of the tumor showed myxomatous change.

Rosinski¹¹⁵ removed a tumor the size of an egg from the left inguinal region of a patient, aged 54. A half a year later he

removed a cystic tumor the size of a plum from the left inguinal region of the same patient. Both tumors were attached to the round ligament and both proved, on microscopic examination, to be adenomyoma.

Sänger.¹¹⁷ A patient, aged 22, para-III, had had a swelling the size of a pigeon's egg in the right inguinal region for a number of years. It had been diagnosed a hernia. During the last three or four months, in connection with pregnancy, the tumor had increased rapidly in size. At operation a fibrosarcoma was removed which had originated in the extraperitoneal portion of the right round ligament.

Spencer-Wells.¹²⁶ Case (a). A patient, aged 50, had noticed a slowly growing, hard tumor in the right inguinal region for a year. A fibroma of the right round ligament, the size of a coconut, was removed.

Spencer-Wells.¹²⁶ Case (b). A patient, aged 40, had noticed a slowly growing, hard tumor in the right inguinal region for three years. A fibroma of the round ligament, the size of an orange, was removed.

Verneuil.¹³⁸ A patient, aged 26, para-I, noticed a small hard tumor in the right inguinal region six weeks after delivery. It grew very slowly and was painful only at the time of menstruation. It was diagnosed a hernia of the ovary or a hydrocele of the canal of Nuck. At operation, a fibroma was found springing from the round ligament.

Nebesky⁹⁴ and Prang¹⁰⁷ have each reported a case of a fibroma arising in the extraperitoneal portion of the round ligament and then growing back into the abdomen, instead of forward into the labium majus, as is usual; while Leopold⁸⁰ has reported a case in which such a tumor grew upward "between the layers of the abdominal wall." As these can hardly be considered vulval tumors they will not be reported.

GROUP III. FIBROID TUMORS ORIGINATING IN THE SUBPERITONEAL CONNECTIVE TISSUE AND APPEARING AT THE VULVA.

Subperitoneal fibromata are the largest tumors known to pathology. The largest ever reported weighed 268 pounds (Buckner¹⁰). The entire subject, including this case, was admirably reviewed by Whitney and Harrington¹⁴¹ in 1905.

These tumors develop in the retroperitoneal connective tissue of the pelvis and growing along lines of least resistance are usually first noticed in the region of the labium majus. Later they are often complicated by further growths in the ischio-rectal region, buttock or groin. More often than not there is more than one growth and it has been noted that in these cases each tumor possesses a pedicle which may be followed up along the vagina or through one of the bony foramina to a common point of origin in the subperitoneal connective tissue of the pelvis.

Clinically, these cases may be considered vulval fibroids, although they do not originate in the connective tissue of the vulva. In each of the following cases the tumor first noticed was a vulval tumor.

Bigelow.¹² A patient, aged 31, had noticed a swelling in the left groin two years previously, which had gradually grown downward, invading the left labium majus and buttock. Examination showed a lobulated tumor the size of a coconut occupying the left labium and buttock and extending up the vagina to the cervix. Microscopic diagnosis, fibroma.

Czyzewicz³¹ removed a small myxofibroma from the region of the mons Veneris of a patient, aged 40. Eight years later she

returned with a large firm tumor of the abdominal wall, extending from the symphysis to the umbilicus. It had been present one year. Microscopic examination showed it to be a fibromyoma.

Edge³⁸ removed a firm tumor from the left labium majus and ischio-rectal fossa of a patient, aged 35. The tumor was the size of an orange, reached up to the uterus and proved on microscopic examination to be a fibroma.

Esmarch.⁴⁰ In 1872, a patient, aged 30, noticed a small swelling in the left labium majus which gradually increased in size. Three years later another tumor appeared in the right buttock and a third in the right groin. In 1876, examination showed: (a) A firm elastic tumor of the right labium majus, the size of a child's head, with a pedicle reaching up into the pelvis along the vaginal wall. (b) A similar tumor hung from the right buttock by a thick pedicle, this mass being the size of a man's head. (c) In the right inguinal region there was an irreducible tumor, the size of a fist, lying above Poupart's ligament. An attempt was made to remove the tumors of the buttock and labium but was unsuccessful. However, they were shown to be composed of myxomatous tissue. In 1877, the tumor of the right groin, which had recently grown rapidly, was removed, and a pedicle, two finger-breadths thick, which extended toward the peritoneum, was cut off as high as possible. In 1886, nine years later, and 14 years after the first tumor was noticed, the patient returned with a recurrence of the tumor of the groin, now in association with an inguinal hernia. The tumor of the buttock now hung below the knees and measured 62 cm. in circumference. The tumor of the labium had grown to the size of a man's head.

Fleming⁴³ operated on a patient, aged 20, for a tumor of the upper end of the right labium majus which had first been noticed four months previously. The tumor was separated from the wall of the vagina and the labium, but a considerable portion was found "passing up toward the sacro-sciatic ligament." A section showed it to be a "fibro-cellular tumor."

Gallet⁴⁸ describes a case occurring in a woman, aged 38, with a firm tumor occupying the whole left labium majus, a similar tumor the size of a man's head on the left buttock and just above it a third, smaller tumor of the same nature. At operation, the vulval growth was found to spring from a pedicle which continued up beneath the ramus of the pubes. The smaller growth on the buttock was found to be lobulated and to be attached to a pedicle which entered the obturator foramen. The largest tumor weighed 1800 gm. The patient died and at autopsy the pedicles of all three tumors were found to connect with a similar tumor in the left side of the pelvis, which was not connected with the pelvic organs in any way. Section showed the tumors to be fibromata containing many small cystic cavities.

Harrington⁶³ removed a pedunculated fibroma, the size of a foetal head at term, from the left labium majus of a patient, aged 46. Six years later the patient returned with a smaller tumor hanging from the left labium and a pedunculated tumor of the same nature hanging from the left buttock and measuring 18½ inches in circumference. The patient was suffering from retention of urine. A catheter showed the bladder to be drawn over toward the large posterior tumor. Both tumors were removed and at the end of five years there had been no recurrence. Microscopic diagnosis, fibroma.

Kaan.⁶⁹ A patient, aged 20, para-II, had noticed a slowly growing tumor in the left labium majus for five years. Examination showed a tumor the size of a fist, hanging between the thighs and a portion of it extending up the left side of the vagina into the pelvic cavity, where it was connected with a mass the size of a six months' pregnancy. At autopsy, the growth was found to have taken its origin in the subperitoneal connective tissue. Microscopic diagnosis, oedematous fibroma.

Kuster.⁷⁴ A patient, aged 42, had noticed a small nodule in the left labium majus and two nodules the size of hazelnuts, just to

the left of the anus, one year previously. Their growth had been so rapid that locomotion was now interfered with. Examination revealed a large soft tumor of the labium which was definitely lobulated and could be followed to the anus. Microscopic diagnosis, fibroma.

MacEwen³¹ removed a tumor weighing three pounds from the left labium majus of a patient, aged 49, para-IX, which had been present nine years. The author considered it to have originated in the ischio-rectal fossa and to have extended from there into the labium and also upward, perforating the levator ani muscle and fascia, and then growing in front of the bladder. Microscopic diagnosis, œdematous fibroma.

Malcolm⁸⁴ describes the case of a patient, aged 30, para-I, with three large fibroid tumors, all uniting in the left side of the pelvis. There was, first, a tumor 7½ inches long distending the perineum; second, a tumor of the buttock 37½ inches long; and third, a large, ill-defined abdominal tumor. The peritoneal tumor was found to be "firmly fixed to the fascia covering the muscles of the anterior lateral wall of the pelvis" and for this reason the author considers it to have taken origin in the fascial tissue. (On account of the typical description given, I feel justified in including this case among the subperitoneal tumors.)

Von Langenbeck.⁷⁷ Case (a). A patient, aged 20, noticed a lump the size of a hazelnut in the right labium majus following trauma. Three years later she had a growth the size of a man's head in the labium and perineum, compressing the vagina and rectum and extending up into the pelvis. In extirpating it a small piece was left adherent to the peritoneum above. The rectum and vagina were intimately adherent. Microscopic diagnosis, œdematous fibroma.

Von Langenbeck.⁷⁷ Case (b). A patient, aged 36, first noticed a small tumor of the perineum which had grown to the size of two fists within a year. It was found to be distending the perineum, the lower portion of the right labium majus and the adjacent skin of the thigh. The vagina was pushed to the left and the tumor was found to extend up into the pelvis. At operation it was necessary to dissect it from the vagina and rectum. Microscopic diagnosis, œdematous fibroma.

Sympton¹²⁹ removed a tumor weighing one pound three ounces from a woman, aged 43, who had noticed it for 18 months. One process passed forward along the vagina into the labium majus and another, upward and backward, very deeply along the rectum, to which it was attached. It was also attached to the sacro-sciatic ligament and to the coccyx. It measured 9 by 4 inches. Microscopic diagnosis, fibroma.

The following cases are of interest as vulval fibroids, but it is questionable whether separate groups should be made of them. Fromme⁴⁵ describes a large tumor of the labium majus which proved to be a fibromyoma containing glandular elements and which he considers to have originated in Bartholin's gland. In this connection it should be remembered that an adenomyoma of the extraperitoneal portion of the round ligament may grow outward, into the labium majus, and appear as a labial growth. Morestin⁹² has advanced the view that a fibroma may develop during the organization of a hematoma, while Kewisch⁷¹ claims that they may develop from either the pelvic fascia or the periosteum of the pelvic bones. The connective tissue of the rectovaginal septum has also been noted as a point of origin. It cannot be denied that these are possibilities, but cases which might be considered as belonging to these groups are very rare.

The following cases have been reported:

GROUP IV. FIBROID TUMORS ORIGINATING IN THE CONNECTIVE TISSUE OF BARTHOLIN'S GLAND.

Fromme.⁴⁵ A patient, aged 18, had noticed a small tumor of the right labium majus a year and a half previously. During the last six months it had grown to the size of a fist. Examination showed a large bluish mass occupying the entire right labium, and forcing the vaginal outlet to the left. It lay immediately beneath the skin. Microscopic examination revealed a connective-tissue tumor containing a few smooth muscle fibers and some fat. Single tubular glands were scattered throughout the entire growth. They were lined with a single layer of epithelium and gave evidence of being offshoots of Bartholin's gland.

Lala⁷⁵ reports a tumor of the right labium majus, which from its situation may have been a case similar to that of Fromme. The tumor, "chiefly of fibro-plastic tissue," was "encysted" in the right labium majus and obstructed the vagina.

Piering¹⁰⁴ removed a rather soft tumor the size of a man's fist which occupied the position of the right Bartholin gland and preceded, for some years, an abscess of the gland. Microscopic examination showed a very cellular fibroma in which there was a single area of hyaline degeneration. This tumor may have originated in the subcutaneous tissue.

Von Recklinghausen¹³¹ removed a tumor of Bartholin's gland which showed a marked thickening of the interstitial connective tissue.

GROUP V. FIBROID TUMORS ORIGINATING IN HÆMATOMATA.

Demarquay⁹⁴ removed a fibrolipoma from the labium majus which had developed after trauma to that labium. The tumor had begun to increase in size and become painful at the time of menstruation.

Morestin⁹² reports a case in which a fibroma the size of a hen's egg developed in a hæmatoma in the right labium majus, following trauma. The appearance was remarkably like that of a scrotum.

These two cases may, of course, be considered as belonging to Group I.

GROUP VI. FIBROID ORIGINATING IN THE RECTOVAGINAL SEPTUM.

Bryant.¹⁵ A patient, aged 40, had had a painless tumor at one side of the perineum, for two years. At operation it was found to be compressing both the vagina and rectum and was enucleated from between them. The tumor was 6 inches long and proved to be an œdematous fibroma.

Smith¹²⁴ removed a soft fibroma the size of a goose's egg from the perineum of a woman, aged 37, para-II. It was firmly embedded in the rectovaginal septum, weighed four ounces, and one process was adherent to the rectum for five inches. Another prolongation was adherent to the vagina.

SUMMARY.

Fibroid tumors of the vulva are the commonest of the benign solid tumors of this region and grow to larger size than superficial fibroid tumors in any other part of the body. As a rule they grow rapidly and soon become pedunculated. Most of them show some form of degenerative change.

The subperitoneal fibromata, which take origin in the pelvic connective tissue and, growing along lines of least resistance, first appear at the vulva, are the largest tumors on record. The

largest tumor ever described was one of this type (Buckner,¹⁹ Whitney and Harrington¹⁴¹), and weighed 268 pounds.

Excluding the subperitoneal group, it may be said that, roughly, two-thirds of the fibroids of the vulva originate in the subcutaneous connective tissue and one-third in the extra-peritoneal portion of the round ligament, *while nearly one-fifth of them become sarcomatous.*

The vascular changes accompanying menstruation and pregnancy are shared by these tumors and exert a marked influence upon them, as is clearly shown by their swelling and sensitiveness under these circumstances. Herein lies the explanation of the fact that, almost without exception, they occur in the child-bearing period, that they grow rapidly, that they usually show degenerative changes and, finally, that a remarkably large percentage of them become sarcomatous.

I wish to take this opportunity to express my appreciation to Dr. Howard A. Kelly, not only for the privilege of reporting these cases, in whose clinic at The Johns Hopkins Hospital they occurred, but mainly for the inspiration and stimulus which the years of close association with his untiring work have always meant to his assistants.

BIBLIOGRAPHY.

1. Albert: Inaug. Diss., Leipzig, 1908.
2. Amaurel: Thesis, Paris, 1883.
3. D'Ambrosio: Giorn. internat. delle scionze med., 1880. Quoted by Esser.⁴¹
4. Arcangelis: Archiv di Ostet. e Gin., 1905, XII, p. 1.
5. Aschoff: Monatsschr. f. Geb. u. Gyn., 1899, IX, p. 25.
6. Aulhoon: Ges. f. Geb. Gyn. zu Leipzig, April 25, 1910.
7. Aumoine: Thesis, Paris, 1876.
8. Backman: Finska lak-sallsk handl., Helsingfors, 1911, II, pp. 332-334.
9. Baer: Am. J. Med. Sc., Phila., 1882, n. s., XXXIII, p. 439.
10. Bell: J. of Obst. and Gyn. of the Brit. Emp., Nov., 1907.
11. Bethège: Bull. de la soc. anat., II, 2me série, p. 395.
12. Bigelow: Boston Med. and Surg. J., 1875, XCII, p. 301.
13. Bindemann: Inaug. Diss., Erlangen, 1894. Ref. Frommel's Jahresb. f. Geb. u. Gyn., 1895, IX, p. 244.
14. Blisner: Ref. Centralbl. f. Gyn., 1910, No. 4, p. 117.
15. Boschenski: Przegląd Lekarski, 1901, p. 103; Ref. Frommel's Jahresb. f. Geb. u. Gyn., 1901, XV, p. 521; also, Centralbl. f. Gyn., 1909, IX, p. 317.
16. Bondi: Ges. f. Gyn. zu Wien, März, 1907. Ref. Gyn. Rundsch., 1907, Pt. I, p. 896.
17. Bovée: Am. J. of Obst., May, 1903, XLVII, p. 674.
18. Bryant: Trans. Path. Soc., London, 1865-66, XVII, p. 276.
19. Buckner: Ohio State Med. Soc. Transactions, 1851.
20. Bullard: Bull. Woman's Hospital, N. Y., 1915, I, pp. 42-48.
21. Burgio: Arch. de Obst. e. Gin., VI, p. 475.
22. Burr: N. Y. and Phila. Med. J., XXXI, 1905, p. 340.
23. Calmann: Deutsche Med. Wochenschrift, Mai, 1905, XXXI, Pt. I, p. 853.
24. Canuyt et Princetau: J. de méd. de Bordeaux, 1912, XLII, p. 556.
25. Cernezz: Pensieri med., Milano, 1914, IV, p. 709.
26. Churchill: Phila., 1857, p. 50.
27. Clark: Univ. of Penn. Med. J., 1901, XIV, p. 78.
28. Coates: Cleveland J. of Med., Jan., 1900, V, p. 24.
29. Collyer: Am. J. of Obst., 1889, XXII, p. 1251.
30. Cullen: Johns Hopkins Hosp. Bull., May and June, 1896.
31. Czyzewicz: Wiener klin. Wochenschrift, 1908, XXI, Pt. 2, p. 1341.
32. Daxl: Diss., Berlin, 1907.
33. Delbanco: Biol. Abt. d. Aerzte v. Hamburg, Mai, 1907, Frommel's Jahresb. f. Geb. u. Gyn., 1907, XXI, p. 156.
34. Demarquay: Soc. de chirurgie, Juillet, 1864.
35. Doorman: Nedrl. tydschr. v. Verlosk. en Gyn., III, No. 3; ref. Centralbl. f. Gyn., 1892, p. 375.
36. Dreyfus: Diss. Strassburg, 1903.
37. Duplay: Arch. gén. de méd., 1882, I, p. 157.
38. Edge: Med. Press and Circ., London, 1896, p. 79.
39. Eichholz: Frauenarzt, 1892, VII, p. 519.
40. Esmarch: Inaug. Diss., Kiel, 1888. Quoted by Whitney.
41. Esser: Inaug. Diss., Bonn, 1892. Ref. Centralbl. f. Gyn., 1892, XVI, p. 871.
42. Fischer: Monatsschr. f. Geb. u. Gyn., 1897, V, p. 317.
43. Fleming: Dublin Quarterly J., 1854, XVII, p. 225.
44. Formad: Phila. Med. Times, 1880, XI, p. 184.
45. Fromme: Monatsschr. f. Geb. u. Gyn., 1904, XX, p. 961.
46. Fuchs: Sammelb. d. Jah. 1911; Gyn. Rundsch., 1912.
47. Fürst: Arch. f. Gyn., XXVII, p. 102. Centralbl. f. Gyn., 1885, IX, p. 478.
48. Gallet: Allg. Wien. med. Zeitschr., 1898, XLIII, p. 86.
49. Gangolphe: Lyon méd., 1884, XLVI, p. 281.
50. Garrigues: N. Y. Med. J., 1884, XXXIX, p. 477.
51. Geldner: Inaug. Diss., Greifswald, 1897.
52. Gemmel: Brit. Med. J., 1906, I, p. 1041.
53. Géroulanos: Orient. med., Février, 1906. Ref. Centralbl. f. Gyn., 1907, XXXI, No. 1.
54. Gfroerer: Diss., Tübingen, 1893.
55. Giles: Trans. of the Obst. Soc. of London, XXXIX, July 7, 1897.
56. Goldreich: Mittl. d. Ges. f. Inn. Med. u. Kinderheilkunde i. Wien, VIII, 1909, Beibl., p. 53.
57. Graefe: Centralbl. f. Gyn., 1897, XXI, p. 105.
58. Grigorowitsch: Wratsch, 1905, fasc. 16. Ref. Revue de Gyn., 1905, IX, No. 5, p. 924.
59. Grime: Glasgow Med. J., 1871, III, p. 265.
60. Guinard: Revue de chir., 1898, IX, p. 63.
61. Handfield-Jones: Trans. Obst. Soc. of London, 1905, XLVII, p. 362.
62. Hansemann: Centralbl. f. Gyn., 1896, p. 279.
63. Harrington: Annals of Surg., 1905, XLI, p. 835.
64. Hecker: Inaug. Diss., 1882. Quoted by Nebesky.⁹⁴
65. Heydemann: Deutsche Zeitschr. f. Chir., 1905, XLI, p. 425. Quoted by Nebesky.⁹⁴
66. Hofmorkl: Centralbl. f. Gyn., 1883, VII, p. 229.
67. Holzmänn: Inaug. Diss., Marburg, 1896. Ref. Jahresb. f. Geb. u. Gyn., 1896, X, p. 265.
68. Ill: Am. J. of Obst., Nov., 1900, p. 654.
69. Kaan: Quoted by Whitney and Harrington.¹⁴¹
70. Kayser: Med. Gesellsch. zu Giessen. Deutsche med. Wochenschrift, 1893, XIX, No. 45, p. 1135.
71. Kewisch: Quoted by Schumann.¹²¹
72. Kirchoff: Centralbl. f. Gyn., XVII, p. 1037.
73. Klob: Pathologische Anatomie der Weiblichen Sexualorgane, Wien, 1864.
74. Küster: Quoted by Whitney and Harrington;¹⁴¹ also by Stein in "Beiträge zur Kenntnis der extraperitoneal Beckentumoren." Inaug. Diss., Berlin, 1876.
75. Lala: Bull. de la soc. anat., 1856, p. 107.
76. Landau: Berl. klin. Wochenschr., Mai, 1902, XXXIX, p. 505.
77. Von Langenbeck: Quoted by Whitney and Harrington;¹⁴¹ also by Esser.⁴¹
78. Largeau: Arch. prov. de chir., Paris, 1892, I, p. 335.
79. Legneu et Morel: Ann. de Gynéc, Février, 1905.
80. Leopold: Arch. f. Gyn., 1880, XVI, p. 402.



FIG. 1.—Case I. Pedunculated fibroma of the labium majus.



FIG. 2.—Case III. Pedunculated fibroma of the labium majus.



FIG. 3.—Case IV. Section of a fibromyxosarcoma of the labium majus.

81. MacEwen: Brit. Med. J., Nov. 28, 1908, Pt. 2, p. 1607.
82. McClintock: Dublin Quar. J., XXXIII, 1862, p. 209.
83. McDonald: Edinburgh Obst. Soc., Dec., 1905, Lancet, Dec. 30, 1905.
84. Malcolm: Lancet, Oct. 14, 1911, Pt. 2, p. 1075.
85. Marcano: Bull. de la soc. anat., 1873, p. 388.
86. Von Mars: Monatsschr. f. Geb. u. Gyn., 1900, XII, p. 1.
87. Mauclair: Ann. de Gyn. et d' Obst., XL, 1893, p. 409.
88. Merkel: Münch. med. Wochenschr., 1901, CCCCLXXXII, No. 44, p. 1774.
89. Michon: Bull. de la soc. anat., 1839, XIV, p. 69. Quoted by Gangolphe.⁴⁹
90. Mond: Centralbl. f. Gyn., 1907, XXXI, p. 344.
92. Monod: Progrès médical, 29 Avril, 1876.
93. Morestin: Bull. et mém. de la soc. anat., 1898, XII, 5me série, p. 526. Ref. Frommel's Jahresb., 1900, p. 439.
94. Nebesky: Monatsschr. f. Geb. u. Gyn., 1903, XXVII, p. 441.
95. Newman: Trans. Chicago Gyn. Soc., Nov. 19, 1897. Ref. Am. Gyn. and Obst. J., 1898, XII, No. 2, p. 230.
96. Odebrecht: Zeitschr. f. Geb. u. Gyn., 1890, XIX, p. 301.
97. Oreillard: Arch. de Tocol. et de Gyn., Dec., 1893, XX, p. 941.
98. Orloff: Wratsch, No. 21. Ref. Frommel's Jahresb., 1900, XIV, p. 526.
99. Paletta: Thesis, 1876, Actes de l'Institut Italien, I, p. 101. Quoted by Aumoine.⁷
100. Parsons: Trans. Obst. Soc. of London, 1906, XLVIII, p. 184.
101. Pavlovski: Terap. Oboz, Odessa, 1912, V, p. 484.
102. Penrose: Am. J. of Obst., 1896, XXXIV, p. 72.
103. Perewaloff: Wratsch Gaz., No. 45, 1911. Ref. Frommel's Jahresb. f. Geb. u. Gyn., 1911, p. 198.
104. Piering: Prager med. Wochenschr., 1896, XXI, p. 189.
105. Polailon: Gaz. méd. de Paris, 1891, No. 32, VII, p. 377.
106. Ponzian: Ann. di Ostet. e. Gin., Milano, 1915, I, pp. 1-9.
107. Prang: Inaug. Diss., Königsberg, 1900, quoted by Nebesky.⁹⁴
108. Prochownik: Centralbl. f. Gyn., 1907, XXXI, p. 345.
109. Prokess: Koezkhóházi, Orvostársulat, Okt. 27, 1896. Ref. Frommel's Jahresb. d. Geb. u. Gyn., 1897, XI, p. 492.
110. Reboul: Bull. de la soc. anat., 1888, II, 5me série, p. 747.
111. Von Recklinghausen: Wiener klin. Wochenschr., 1899, No. 2, XII, quoted by Fromme.⁴⁵
112. Reverdin: Rev. de la Suisse Romande, 1894, XIV, p. 466.
113. Ritchie: Glasgow Obst. and Gyn. Soc.; ref. J. of Obst. and Gyn., Dec., 1904.
114. Rosenthal: Monatsschr. f. Geb. u. Gyn., 1911, XXXIII, p. 235.
115. Rosinski: Centralbl. f. Gyn., 1899, XXIII, p. 1545.
116. Rouston: Montpellier méd., Février, 1884.
117. Sängér: Arch. f. Gyn., 1880, XVI, p. 258.
118. Von Scanzoni: 4th Am. Ed., p. 587.
119. Schiele: Inaug. Diss., Erlangen, 1882.
120. Schneider-Sievers: Centralbl. f. Gyn., 1907, XXXI, p. 345.
121. Schumann: Am. J. Med. Sc., 1907, CXXXIII, p. 448.
122. Schwaiblmaier: München, 1912, Müller u. Steinicke, p. 19.
123. Selke: Münch. med. Wochenschr., No. 38, Sept. 19, 1905, p. 1851.
124. Smith: Am. J. Obst., 1897, XXXV, p. 128.
125. Souligoux: Ann. de Gyn., LIII, Mars, 1900.
126. Spencer: Trans. Path. Soc., London, 1866, XVII, p. 188. Brit. Med. J., Nov. 4, 1865.
127. Storer: Boston Med. and Surg. J., 1864, LXXI, p. 478.
128. Strina: La Rassegna d' Ostetr. e. Gin., Napoli, 1911, XX, No. 2, p. 65.
129. Sympton: Brit. Med. J., 1867, I, p. 80. Lancet, 1905, Dec. 30, Pt. 2, p. 1897.
130. Szili: Beiträge z. klin. Chir., 1901, XXXI, No. 3, p. 734.
131. Tarnier: Virchow-Hirsch's Jahrbücher, 1872, p. 659. Gaz. des hôp., No. 32.
132. Thomas: Centralbl. f. Gyn., 1902, XXVI, No. 25, p. 657.
133. Von Tischendorf: Centralbl. f. Gyn., 1888, XII, p. 476.
134. Tuttle: Am. J. of Obst., 1891, XXIV, p. 714.
135. Valude: Progrès méd., 1884, XII, No. 44, p. 868.
136. Van der Smissen: Progrès méd. Belge, 1900, I, p. 20.
137. Veit: Handbuch der Gynäcologie, Bd. IV, 2te Hälfte, p. 712.
138. Verneuil: Arch. gén. de méd., 1882, I, p. 263.
139. Villiers, de Hotman and Damage: Arch. de soc. et de gin., Février, 1893, XX, p. 129.
140. Weber: Monatsschr. f. Geb. u. Gyn., 1899, IX, p. 591.
141. Whitney and Harrington: Annals of Surg., 1905, XLI, p. 823.
142. Zabaroff: Thèse de Paris, 1898.
143. Zangemeister: Monatsschr. f. Geb. u. Gyn., 1906, XXIII, p. 125.
144. Zielewicz: Deutsche med. Wochenschr., 1886, XII, No. 24, p. 409.
145. Ziembycki: Wien. klin. Wochenschr., 1809, CCXII, p. 1341.
146. Zubrzycki: Tyg. lekarsk, 1910, No. 41, p. 593. Ref. Jahresb. f. Geb. u. Gyn., 1910, XXIV, p. 222, by Neugebauer.

BOOKS RECEIVED.

- The New Method in Diabetes.* The Practical Treatment of Diabetes as Conducted at the Battle Creek Sanitarium, Adapted to Home Use, Based Upon the Treatment of More than Eleven Hundred Cases. By J. H. Kellogg, M. D., LL. D. 1917. 12°. 177 pages. Good Health Publishing Co., Battle Creek, Michigan.
- An Inquiry into the Principles of Treatment of Broken Limbs.* A Philosophico-Surgical Essay, with Surgical Notes. By William F. Fluhrer, M. D. 1916. 8°. 128 pages. Rebman Company, New York.
- The Respiratory Exchange of Animals and Man.* By August Krogh, Ph. D. With diagrams. 1916. 8°. 173 pages. Longmans, Green & Co., London.
- A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology.* By Torald Sollmann, M. D. Illustrated. 1917. 8°. 901 pages. W. B. Saunders Company, Philadelphia and London.
- Congress of American Physicians and Surgeons.* Transactions. Tenth triennial session held at Washington, D. C., May 9 and 10, 1916. 1917. 8°. 149 pages. New Haven, Conn.
- Board of Health of the Territory of Hawaii, Bureau of Vital Statistics.* Report of the Registrar General for the Fiscal Year Ended June 30, 1916. 4°. 76 pages.
- A Laboratory Guide in Pharmacology.* By Torald Sollmann, M. D. Illustrated. 1917. 8°. 354 pages. W. B. Saunders Company, Philadelphia and London.
- Microbiology. A Text-Book of Microorganisms General and Applied.* Edited by Charles E. Marshall. Second edition, revised and enlarged with 186 illustrations. 1917. 12°. 900 pages. P. Blakiston's Son & Co., Philadelphia.
- Military Surgery.* By Dunlap Pearce Penhallow, S. B., M. D. (Harv.) With Introduction by Sir Alfred Keogh, K. C. B. Original drawings by the author. 1916. 8°. 432 pages. Henry Frowde, London; Hodder & Stoughton, London.

- Central Indiana Hospital for the Insane.* Report from the Department of Pathology and the Department of Clinical Psychiatry. Central Indiana Hospital for the Insane. 1913-1914 and 1914-1915. Vol. VI. 1916. 8°. 670 pages.
- A Reference Handbook of the Medical Sciences.* Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. By various writers. First and second editions edited by Albert H. Buck, M. D. Third edition completely revised and rewritten. Edited by Thomas Lathrop Stedman, A. M., M. D. Complete in eight volumes. Volume VII. Illustrated by numerous chromolithographs and 469 half-tone and wood engravings. 1917. 4°. 992 pages. William Wood Company, New York.
- For and Against Experiments on Animals.* Evidence before the Royal Commission on Vivisection. By Stephen Paget, F. R. C. S. With an introduction by the Right Hon. the Earl of Cromer, O. M., G. C. M. G., G. C. B. 1912. 12°. 344 pages. Paul B. Hoeber, New York.
- The Growth of Medicine.* From the Earliest Times to about 1800. By Albert H. Buck, B. A., M. D. 1917. 8°. 582 pages. Yale University Press, New Haven, Humphrey Milford, London.
- United States, Department of Commerce. Bureau of the Census.* United States Life Tables, 1910. Prepared under the supervision of Prof. James W. Glover of the University of Michigan. Sam L. Rogers, Director. 1916. 4°. 65 pages. Government Printing Office, Washington.
- Public Health Reports.* Issued Weekly by the United States Public Health Service. Containing Information of the Current Prevalence of Disease, the Occurrence of Epidemics, Sanitary Legislation, and Related Subjects. Vol. XXXI, Part 1, Nos. 1-26, January-June, 1916. 8°. 1745 pages. Government Printing Office, Washington.
- United States, Department of Commerce. Bureau of the Census.* Mortality from Cancer and Other Malignant Tumors in the Registration Area of the United States, 1914. Sam L. Rogers, Director. 1916. 4°. 212 pages. Government Printing Office, Washington.
- Clinical Tuberculosis.* By Francis Marion Pottenger, A. M., M. D., LL. D. With a Chapter on Laboratory Methods by Joseph Elbert Pottenger, A. B., M. D. Volume I. *Pathological Anatomy, Pathological Physiology, Diagnosis and Prognosis.* With one hundred and five text illustrations and charts, and six plates in colors. Volume II. *Complications and Treatment.* With 62 text illustrations and charts, and four plates in colors. 1917. 8°. C. V. Mosby Company, St. Louis.
- Cancer Commission of Harvard University.* Fourth Annual Report of the Collis P. Huntington Memorial Hospital for Cancer Research and of the Laboratories of the Cancer Commission of Harvard University. 1915-1916. (For the year ending June 30, 1916.) 8°. 63 pages. Boston.
- Royal Victoria Hospital, Montreal.* Scientific Reports. Series B. No. 1. Edited by George E. Armstrong, Charles F. Martin, W. W. Chipman, W. G. M. Byers, Horst Oertel, editorial committee of the board. 1916. 4°. 211 pages. Gazette Printing Company, Limited, Montreal.
- New York City, Department of Health.* Annual Report for the calendar year 1915. 1916. 4°. 219 pages. New York City.
- Text-Book of Surgical Operations.* Illustrated by Clinical Observations. By Prof. Fedor Krause, in association with Emil Heymann, M. D. Translated into English and edited for American readers by Albert Ehrenfried, A. B., M. D., F. A. C. S. In six volumes. Volume II. With 373 illustrations in two or more colors. 1917. 4°. 715 pages. Rebman Company, New York.
- Traumatic Surgery.* By John J. Moorhead, B. S., M. D., F. A. C. S. With 522 original illustrations. 1917. 8°. 760 pages. W. B. Saunders Company, Philadelphia and London.
- American Medical Association.* Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1916, with the comments that have appeared in the journal. 1917. 12°. 87 pages. Press of the American Medical Association, Chicago.
- American Pediatric Society.* Transactions. Twenty-eighth session. Edited by Linnaeus Edford La Fetra, M. D. 1916. 8°. 338 pages.
- Organism and Environment as Illustrated by the Physiology of Breathing.* By John Scott Haldane, M. D., LL. D., F. R. S. 1917. 12°. 138 pages. Yale University Press, New Haven.
- Nervous and Mental Disease Monograph Series No. 24. Study of Organ Inferiority and its Psychological Compensation.* A Contribution to Clinical Medicine. By Dr. Alfred Adler. Authorized Translation by Smith Ely Jelliffe, M. D. 1917. 8°. 86 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.
- Nervous and Mental Disease Monograph Series No. 25. The History of the Psychoanalytic Movement.* By Prof. Dr. Sigmund Freud, LL. D. 1916. 8°. 58 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.
- International Clinics.* A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. By Leading Members of the Medical Profession Throughout the World. Edited by H. R. M. Landis, M. D. Volume I. Twenty-seventh series. 1917. 8°. 305 pages. J. B. Lippincott Company, Philadelphia and London.
- American Medical Association.* Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1916 with the Comments that have Appeared in the Journal. 1917. 16°. 87 pages. Press of American Medical Association, Chicago.
- The Value of Blood Pressure in the Diagnosis and Prognosis of Disease.* By Dr. Allen G. Rice. Fiske Fund Prize Essay No. LVI. 1916. 8°. 53 pages. Snow and Farnham Company, Printers, Providence.
- University of Michigan.* Transactions of the Clinical Society. Volume VII. Edited by the Secretary-Treasurer. 1916. 4°. 164 pages. Ann Arbor, Michigan.
- Text-Book of Ophthalmology.* By Hofrat Ernst Fuchs. Authorized translation from the twelfth German edition; completely revised and reset, with numerous additions specially supplied by the author and otherwise much enlarged by Alexander Duane, M. D. With 462 illustrations. Fifth edition. 1917. 8°. 1067 pages. J. B. Lippincott Company, Philadelphia and London.
- American Medical Association.* Transactions of the Section on Genito-Urinary Diseases. 1916. 8°. 350 pages. American Medical Association Press, Chicago.
- The Internal Secretions.* Their Physiology and Application to Pathology. By E. Gley, M. D. Translated from the French and edited by Maurice Fishberg, M. D. Authorized Translation. 1917. 12°. 241 pages. Paul B. Hoeber, New York.
- Cancer, Its Cause and Treatment.* By L. Duncan Bulkley, A. M., M. D. Volume II. 1917. 12°. 282 pages. Paul B. Hoeber, New York.
- Localisation et Extraction des Projectiles.* Par L. Ombrédanne et R. Ledoux-Lebard. Avec 225 figures dans le texte et 8 planches hors texte. 1917. 12°. Masson et Cie., Paris.

Diagnosis from Ocular Symptoms. By Matthias Lanckton Foster, M. D., F. A. C. S. 1917. 8°. 490 pages. Rebman Company, New York.

Clinical Bacteriology and Hematology. For Practitioners. By W. D'Este Emery, M. D., B. Sc. Fifth edition. 1917. 8°. 310 pages. P. Blakiston's Son & Co., Philadelphia.

Rest, Suggestion and Other Therapeutic Measures in Nervous and Mental Diseases. By Francis X. Dercum, A. M., M. D., Ph. D. Second edition. 1917. 8°. 395 pages. P. Blakiston's Son & Co., Philadelphia.

The Diseases of Infancy and Childhood. For the Use of Students and Practitioners of Medicine. By L. Emmett Holt, M. D., Sc. D., LL. D. and John Howland, A. M., M. D. Seventh edition, fully revised. With 215 illustrations. 1916. 8°. 1180 pages. D. Appleton & Company, New York and London.

Principles of Pharmacy. By Henry V. Arny, Ph. G., Ph. D., F. C. S. Second edition, revised. With 267 illustrations. 1917. 8°. 1056 pages. W. B. Saunders Company, Philadelphia and London.

Rockefeller Institute for Medical Research. Studies. Volume XXVI. 1917. 8°. 629 pages. The Rockefeller Institute for Medical Research, New York.

State Board Questions and Answers. By R. Max Goepf, M. D. Fourth edition, thoroughly revised. 1917. 8°. 724 pages. W. B. Saunders Company, Philadelphia and London.

Diseases of the Stomach, Intestines, and Pancreas. By Robert Coleman Kemp, M. D. Third edition, revised. With 438 illustrations. 1917. 8°. 1096 pages. W. B. Saunders Company, Philadelphia and London.

American Therapeutic Society. Transactions. 1916. Editor, A. Ernest Gallant, M. D. 1917. 8°. 237 pages. Published by the Society.

Parke, Davis & Co., Detroit, Mich. Collected Papers from the Research Laboratory. Dr. E. M. Houghton, Director. Reprints. Volume IV. 1916. 8°. 550 pages. Detroit, Michigan.

With a Field Ambulance at Ypres. Being Letters Written March 7-August 15, 1915. By William Boyd. Illustrated. 1916. 12°. 110 pages. George H. Doran Company, New York.

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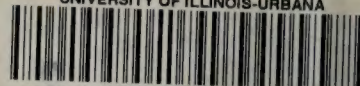
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